THE CANADIAN REGULATORY PROCESS
For Evaluating
Recombinant Bovine Growth Hormone
in the Dairy Industry:
A Critical Review

Toronto Food Policy Council Discussion Paper #12

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This is a work in progress. The main body of this publication flows from six years of research into rbGH by Victor Daniel, a professional in the Ontario dairy industry and co-chair of the Toronto Food Policy Council. The specialized section on Insulin-Like Growth Factor-1 is by Dr. Eve Shullman, an epidemiologist employed for most of her career with Health Canada. The work was endorsed for publication by the Toronto Food Policy Council in June 2000. Please forward any comments or requests for additional copies to the Toronto Food Policy Council, 277 Victoria Street, Room 203, Toronto, ON, Canada, M5B 1W2, or phone 416-392-1107.

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Dedication

To our predecessors on the Toronto Food Policy Council, who believed that a community can hold together and protect what is good.

Preface

> ***"Nothing is more hurtful to the progress of a dairy industry as the ignorance or indifference that allows inferior milk."***
>
> James S. Duff, Minister of Agriculture for the Province of Ontario, "Dairying in Ontario, Canada - A Great Industry," Legislative Assembly of Ontario, 1910.

Milk enjoys a legendary reputation as "nature's perfect food," a wholesome comfort food equated with purity, goodness, health and well-being in "a land of milk and honey." That reputation has been hard-earned, and, until recently, jealously-guarded.

Many people heaved a sigh of relief when Health Canada safeguarded milk's reputation in 1999 by refusing to license one brand of recombinant bovine Growth Hormone (rbGH), a genetically-engineered hormone designed to make cows produce more milk than their normally-inherited abilities allow.

Once this high-profile decision was made, there was a steep drop-off in policy analysis of the nuts and bolts details of the federal government's regulation of both milk and genetic engineering. But taking milk purity for granted is not a good way to treat policy trends that might overturn the protective inheritance from over a hundred years' painstaking work by public health officials, dairy farmers, processors, universities and government regulators.

The aim of this discussion paper is to revive respect for that legacy of public health protection, and to portray how vulnerable that legacy became. Disregard for this legacy brought synthetic rbGH within a regulatory hair's breadth of federal government approval.

In retrospect, what's most alarming about the rbGH controversy is the fact that there was any controversy or indecision at all. When federal government authorities were confronted with an application to license the use of synthetic hormones on dairy cows, they really only had two options. They could have dismissed the application out of hand as a contravention of basic rules; they could have refused to set new rules for matters relating to milk purity and safety, which are largely provincial and municipal responsibilities; they could have refused to tamper with effective and comprehensive policies established by the dairy industry and public health regulators over the course of a century. If federal government authorities chose not to do that, they had only one lawful and logical alternative. They would have begun the stem-to-stern overhaul of an entire system of public health regulation, starting with such basics as the definitions of milk and dairy cattle, the current definitions of which clearly forbid hormone use or contamination.

Instead of following the logic of historical precedents which created progressive legislation, officials in government departments and in the dairy industry itself resorted to piecemeal approaches which threw the legitimacy of a long-established, respected and effective system for ensuring public safety into limbo.

In less precarious times, the specifics around an rbGH application would have been settled definitively and without indecision. A hundred-year history of milk and dairy regulation literally ruled out the possibility of introducing hormones, synthetic or not, in the dairy industry: literally, as in, embedded in the very definitions of milk and dairy cows referenced in countless statutes and codes, and supported by public health regulators and dairy industry participants alike. This discussion paper will review the effective public health safeguards which emerged from the past, and assess the relevance of this tradition to protecting animal and human health today. This paper will also propose measures which federal government departments, in co-operation with public health authorities and participants in the dairy industry, can adopt to ensure that the best practices which have evolved from the past are maintained in the future.

The absence of a thorough and systematic regulatory review process in the case of the rbGH application before Health Canada indicates the stress that the federal government's entire method for evaluating agricultural technologies is under. One notable exception came from the Health Canada scientists who authored the rbST GAPS Analysis Report in 1998. Because mistakes in the government's regulatory system can lead to catastrophic accidents, it is urgent that well-conceived systems for public protection be put in place. The dairy industry, together with provincial and municipal regulators, already provide one model for such a system. That system is analyzed in this paper, with the hope that its traditions can be put to good effect for public health, the environment and the agricultural sector of the future.

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The Toronto Food Policy Council

The Toronto Food Policy Council works to develop a just and sustainable food system. It is charged with a mandate to:

i Reduce hunger, and reliance on charitable food distribution;
ii Increase access to nutritious, affordable, safe and personally-acceptable foods;
iii Promote food production and distribution systems which are nutritionally and environmentally sound.

To achieve these goals, the Toronto Food Policy Council will:

1. Work with community groups on food access issues, sharing information, helping with fundraising and project development, and identifying areas for research;

2. Review government policies and practices, and advise the Board of Health and City Council on social, economic and health policy issues with regard to production, processing, availability, cost, and waste in the food system;

3. Work with other organizations to provide useful educational materials on the food system;

4. Promote policy research on the food system, examining health indicators and actions being taken in other communities which may be applicable to Toronto;

5. Gather information from existing organizations working on food-related issues and communicate this information to the public.

Order of Reference

The Toronto Food Policy Council is a sub-committee of the City of Toronto Board of Health.[1] Established in 1991[2], the Council is a multi-sector citizen's committee including City Councillors, and volunteer representatives of business, farm, consumer, labour, multi-cultural, anti-hunger and community development groups, constituting 21 voting members and three staff.

Pursuant to Toronto Board of Health directives, and support to the Toronto Food Policy Council recommendations regarding recombinant bovine Growth Hormone which have been on file since 1991, responding to the positions of concern of the Association of Local Official Health Agencies[3] (of which the City of Toronto is a member) and other individual Boards of Health[4], and in order to fulfill our commitment to our mandate, this document is a response to Health Canada's decision regarding recombinant bovine Growth Hormone. This document addresses the concerns presented by the afore-mentioned bodies.

Readers should be aware that the lateness of this document is due to the late release of World Health Organization Technical Report Series 888, "Evaluation of Certain Veterinary Drug Residues in Food," which allows Toronto Food Policy Council to fully comment on the entire review process of rbGH. WHO Report 888 is a required reference before any comments can be made on the findings of the Fiftieth Report of the Joint FAO/WHO Expert Committee on Food Additives in April 1998. WHO Report 888 was not released until June of 1999, months after Health Canada made its decision.

[1] TFPC was re-confirmed as a sub-committee of the Board of Health of the new amalgamated Corporation of the City of Toronto, June 23rd, 1998, (item 7), and forwarded this matter to the Council of the Corporation of the City of Toronto, in clause 3, found in Report no. 9 put forward by the Medical Officer of Health and Toronto Food Policy Council, where the mandate, terms of reference and the composition of the Toronto Food Policy Council were adopted without amendment at City Council's meeting July 8th, 9th, and 10th of 1998

[2] Toronto Food Policy Council Policy Manual, Feb., 1995, History of the Implementation of the Toronto Food Policy Council

[3] Resolution No. 7, June 19 -22, 1994 and Resolution A95-4, June 18 -21, 1995,

[4] Motions of the prior Cities of North York, July 10th, 1996, City of Scarborough, Sept, 9th, 1996, and Eastern Ontario Health Unit, Sept. 6th, 1996,

EXECUTIVE SUMMARY

"In order to assess the likely effect of a product, scientists must have some knowledge of the social context into which the drug is to be introduced, and an implicit acceptance of the values inherent in that context." Lisa Nicole Mills, *"Science and Social Context: The Regulation of Recombinant Bovine Growth Hormone (rbGH) in the United States and Canada, 1982-1998."* PhD Thesis, University of Toronto, 1999.

The controversy around recombinant bovine Growth Hormone (rbGH), a genetically-engineered hormone designed to modify a cow to produce milk beyond her inherited or normal capabilities, has been ongoing since the 1980s. The Toronto Food Policy Council has followed this debate for over nine years, and was actively engaged in public discussions around Health Canada's regulation of rbGH. These belabored and often-agonized discussions opened the Food Policy Council's eyes to a severe dysfunction within the regulatory system: long-term memory loss.

What's been called "regulatory drift" had gone so far that by 1999, the year Health Canada made its decision on rbGH, federal health and agricultural officials had lost sight of a precious piece of Canadian public health heritage. The legacy of that heritage was a set of laws and regulations which protected public health on a sound foundation of science-based public policy. In spirit and specific detail, this web of public health regulations prohibited the routine use of any hormone -- genetically-engineered or not -- for milk or meat production in dairy cattle. Yet, no department or expert panel evaluating rbGH assessed the information on rbGH within the context of legislated requirements developed for Canada's progressive dairy industry.

The basic directive of the Canadian dairy cattle industry is to provide the public with the normal lacteal secretion obtained from the mammary gland of a cow, whose biological properties are the result of breeding (male x female) in a licensed environment, producing raw milk to be processed with known and proven procedures, such as pasteurization. The injection or supplementation of rbGH, or even natural bovine Growth Hormone (bGH), alters a cow's physiology. It creates an abnormal biochemical profile in milk, because the cow has been modified to function at a level beyond her inherited capabilities, creating elevated hormone levels in milk and mammary tissue which Canadian law does not recognize.

Our review shows the door must be shut permanently on the routine use of any hormones for milk or meat production in lactating dairy cattle, and that government, university and dairy farm organizations should either respect time-tested regulations or reform them comprehensively. If change is to occur, then more than one regulation at one level of government must change. The laws within different jurisdictions would also have to change if a comprehensive science-based regulatory process is to retain credibility.

Nearly all dairy cattle in Canada exist due to a scientific protocol known as "breed improvement," which is promoted within a federal statute known as the "Animal Pedigree Act," enacted in 1912 to help breed associations develop livestock of superior qualities. The Act is an enablement class statute and is also a statute of definition within the North American Free Trade Agreement. All livestock registered in Canada receive their own sole and permanent registration number within their respective breed associations. It is these registration numbers that act as a benchmark for scientific continuity.

The first registered cattle in Canada were of a breed of cattle known as Shorthorns. A cow named Countess (registration number 782) and her bull calf Leopold (registration number 761) were imported from the United States by Judge Robert Arnold of St. Catherines, Ontario in 1832. (See Marshall, Shorthorn Cattle in Canada, 1932) All registered animals emanate from their respective foundation stock within breed, and the foundation stocks of these breeds were never exposed to a technology that adulterated their physiology. In our view, this serves as a benchmark of integrity proving breeding value for each generation. The use of rbGH, which alters a cow's physiology, would eliminate the empirical integrity of the herdbooks which act as databases.

In the case of dairy cattle, part of proving breeding value is recording the amount of milk a dairy cow produces. Milk recording programs have existed in Canada since 1901. Over the years, these programs evolved, and in 1992 the Canadian Milk Recording Standards included clauses that forbad any practice intended to create an abnormal amount of milk. The non-therapeutic use of rbGH, or even natural bGH, would violate that point of order.

It is not the milk record that serves as evidence, but rather the animal itself. Because dairy cattle are normally registered from birth to three months of age, the assigned milk recording identification number of a cow at the time of her lactation (around two years of age) is linked to her registration number in the herd book. Someone recording the milk of a registered animal which has been modified or adulterated, would, in fact, be recording the wrong animal physiology for scientific evaluation. This negates proof of breeding value, and contravenes the intent of the Animal Pedigree Act. Regrettably, this Act was not mentioned once in the major section on genetics included in the May, 1995 Rbst Task Force Report, despite the fact that this Report was assigned by the Department of Agriculture and Agri-Food, the department responsible for the Act.

The milk from an adulterated dairy cow expresses an abnormal biochemical profile, when compared to milk from a standard-bred cow. This includes an average 200% increase in both Insulin-Like Growth Factor-1 (IGF-1) in milk, and thyroxine-5-monodeiodinase within the mammary tissue of a dairy cow injected with rbGH. Neither increase is normal; nor have we found any scientific evidence that these increases are within normal ranges of bred animals, given the nature of the drug's use, which is non-therapeutic. The human health consequences are unknown. Therefore, rbGH violates the definition of milk in the Food and Drugs Act.

In 1915, at the behest of Dr. Charles Hastings, Chief Medical Officer of Health, Toronto became the first city in Canada to enact compulsory pasteurization of milk to safeguard against contagious diseases then found within milk. Since then, pasteurization has become standard across the country. Presently, there are two legal requirements before milk is considered safe for public consumption. The first is the minimum pasteurization

temperatures, as cited within the Health Protection and Promotion Act of Ontario and the National Dairy Code. The second requirement is proof that pasteurization occurred using the official MFO-3 method, as required by the Food and Drugs Act (Division 8, sect. B.02.002.2) and the Health Protection and Promotion Act of Ontario (section 43 [1] and [2]), as amended July 24, 1998.) The key rbGH studies fail to incorporate these requirements in their study protocols.
In evaluating the scientific claims regarding IGF-1 in milk from rbGH-modified cows, there is a major discrepancy in the readings of pasteurization temperatures. The claim that any elevated levels of IGF-1 would be denatured by pasteurization is not supportable given the failure to reference the fluid milk processing that the public is actually exposed to. The temperatures cited in the scientific literature show IGF-1 being denatured at 250 degrees Fahrenheit for 15 to 20 minutes. Fluid milk for human consumption is only pasteurized in one of two ways: 145 degrees F. for 30 minutes, or 161 degrees F. for 16 seconds and quickly cooled. Neither regulated pasteurization protocol will denature excess
IGF-1.

As a result, consumers, from the farm family to the city dweller, would be exposed to abnormal levels of IGF-l. IGF-1 is a normal constituent of mammalian milk. However, both bovine and human IGF-1 are identical proteins consisting of 70 amino acids, known to regulate biological transport processes, cell division and differentiation as well as tumor establishment and maintenance. The IGF-1 level in standard dairy cows, pre-parturition (colostrum) ranges from 100-300 ng/ml of milk, and from parturition to two weeks afterward ranges from 17-34 ng/ml of milk. Normal milk, from two weeks in a lactation to 305 days (standard lactation length), is 1-5 ng/ml of milk. Scientific literature confirms that during an injection period of rbGH these levels can increase as much as seven-fold. RbGH promoters argue these IGF-1 levels are safe by comparing human breast milk to milk from rbGH-adulterated cows. Human milk is higher in IGF-1 levels than bovine milk, as it is supposed to be. But most people consume cows' milk for a lifetime, while an infant only nurses for a few months or years. This is not a valid comparison.

Although IGF-1 can be dissolved by the gastric juices of the human stomach, milk creates a unique problem because casein is present in milk. Recent literature shows casein protects IGF-1 from being dissolved in the upper gastro-intestinal tract. IGF-1 has a minimum 9% bio-availability to be absorbed into the human body, and casein raises that by 67%. Higher IGF-1 levels are reported to be a risk factor for prostate cancer. Normally, IGF-1 levels are supposed to decline as one ages, but actual patterns of consumption suggest that many will have more, rather than less, exposure in later life if rbGH is ever licensed.

Furthermore, contrary to the arguments of the Joint Expert Committee on Food Additives (JECFA), a continuous low level of IGF-1 can promote cell growth more than temporary high IGF-1 levels. As well, the figures published by the JECFA are for a human consumption rate of 1.5 litres of milk per day, with a half life for IGF-1 of 0.5 to 2.5 hours at one sitting; this ignores the normal patterns of milk consumption, which occur at intervals (meals, snacks) throughout the entire day. This assertion by JECFA has no relevance for real-life experience.

To date, typical regulatory reports have failed to take into account actual patterns of milk consumption. For instance, Canadian farm families are allowed to drink raw unpasteurized milk from their own milk tanks. Farm families, pending the degree of usage of rbGH on the farm, could be exposed to unstable hormone levels resulting from the discretionary use of rbGH by the farm owner. Vulnerable segments within the population - such as pregnant women, the foetus, those with cancer or at risk of cancer, and those suffering with or having a pre-disposition to acromegaly (severe swelling of the hands and feet) and diabetics - were not properly considered.

To predict a potentially adverse effect of a product, population models, as suggested in the above paragraph, must be identified. Toxicological assessments must include the results of acute, sub-acute and chronic (long-term) studies, and two-generation teratological (birth defects) studies. Other necessary studies include proof of the purity of the test substance, which requires a High Performance Liquid Chromatography reading, and residue studies to support regulations on withdrawal periods. The longest human assessment study ever done on rbGH was 90 days, and it failed to demonstrate appropriate references compatible with the requirements of human safety evidence.

Furthermore, the discussion around IGF-1 as a health risk is compromised by the deficiencies in the study protocols. None of the studies replicate what actually happens in a farming operation. Farmers themselves can create fluctuating levels of IGF-1 at their personal discretion. As an example: one year, farmer A may decide to inject 20% of the herd; farmer B, down the road, may decide to inject 60% of the herd; then, farmer A may decide to increase to 50%, and farmer B may decide to restrict use to a few cows. In short, there will be no stability of IGF-1 levels once rbGH is licensed. Regulators paid no attention to this fact of life when designing or evaluating their safety studies.

Finally, Health Canada's integrity has been compromised by reliance on studies that have no constitutional significance. The decision on licensing an rbGH variant currently rests with Health Canada. We have found Health Canada too ready to accept foreign assessments of rbGH, such as the JECFA or, the United States Food and Drug Administration. This conforms to a pattern within globalized, trade regimes to defer to international bodies. Neither JECFA nor the FDA have jurisdiction in Canadian dairy industry affairs. The Expert Panel on Human Safety assigned by Health Canada admitted in writing it would not review rbGH within a dairy regulatory context; therefore, it incorporated findings from studies using inappropriate pasteurization protocols.

Nor does Health Canada have sole jurisdiction in matters relating to milk quality. Milk falls under the jurisdiction of the provinces and, in the case of Ontario, the Ministry of Health, Ontario Ministry of Agriculture, Food and Rural Affairs, the Municipal Health Units and Medical Officers of Health, and Dairy Farmers of Ontario. The federal Department of Agriculture and Agri-Food should have intervened to point out the constitutional basics of regulatory directives in the dairy industry.

To bring an end to regulatory drift, and to restore the basics of Canada's progressive dairy industry and public health laws, we recommend:

1. That dairy livestock be analyzed empirically for breed improvement and production of normal milk, as set out in this report, and that these breeding considerations be incorporated and integrated in all legislation, codes and bylaws relating to dairy cattle and milk;

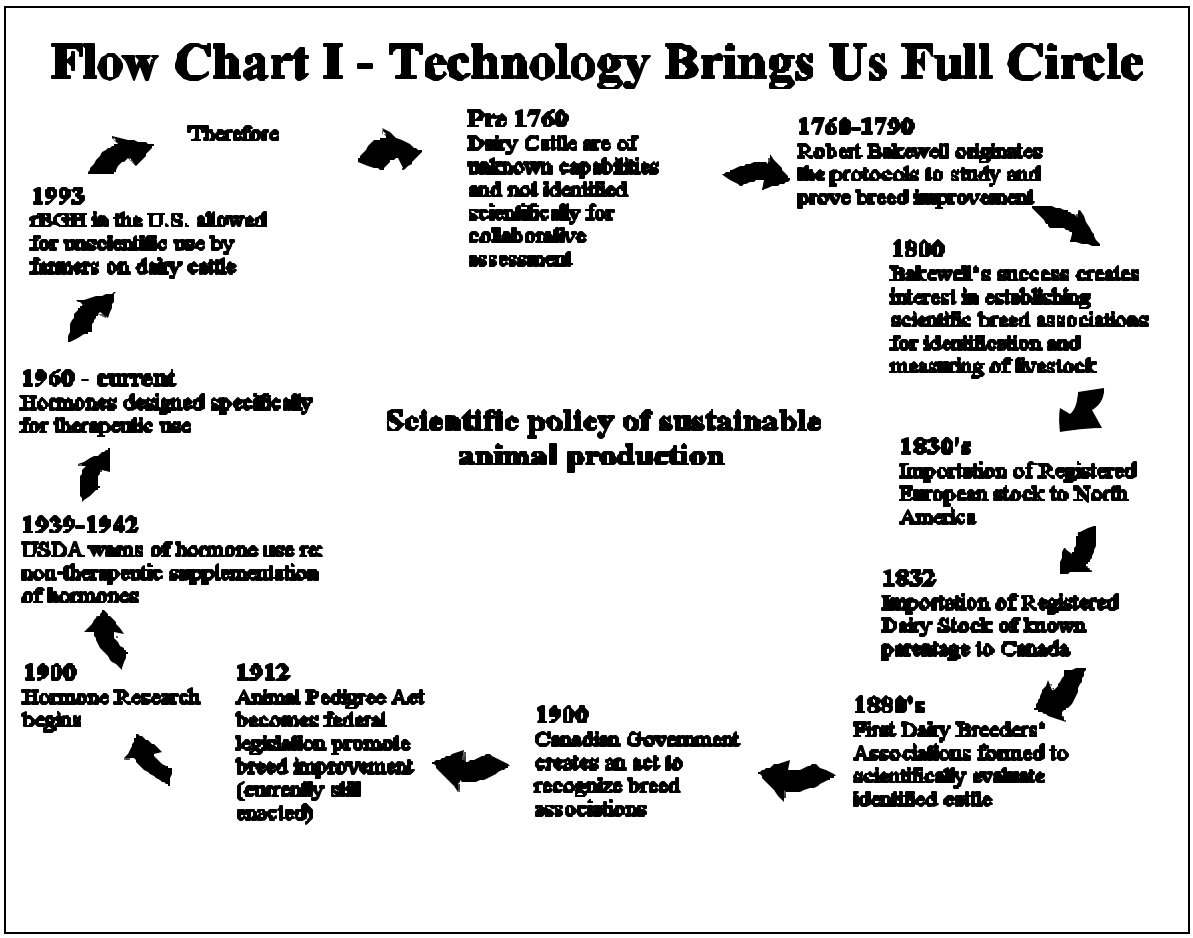
2. That any technology influencing dairy cattle physiology, including genetically-engineered plants, be tested for influences on raw milk and be evaluated in relationships to the usual processing within dairies;

3. That the prohibition against indiscriminate use of any hormone on dairy cattle be confirmed (See Appendix E);

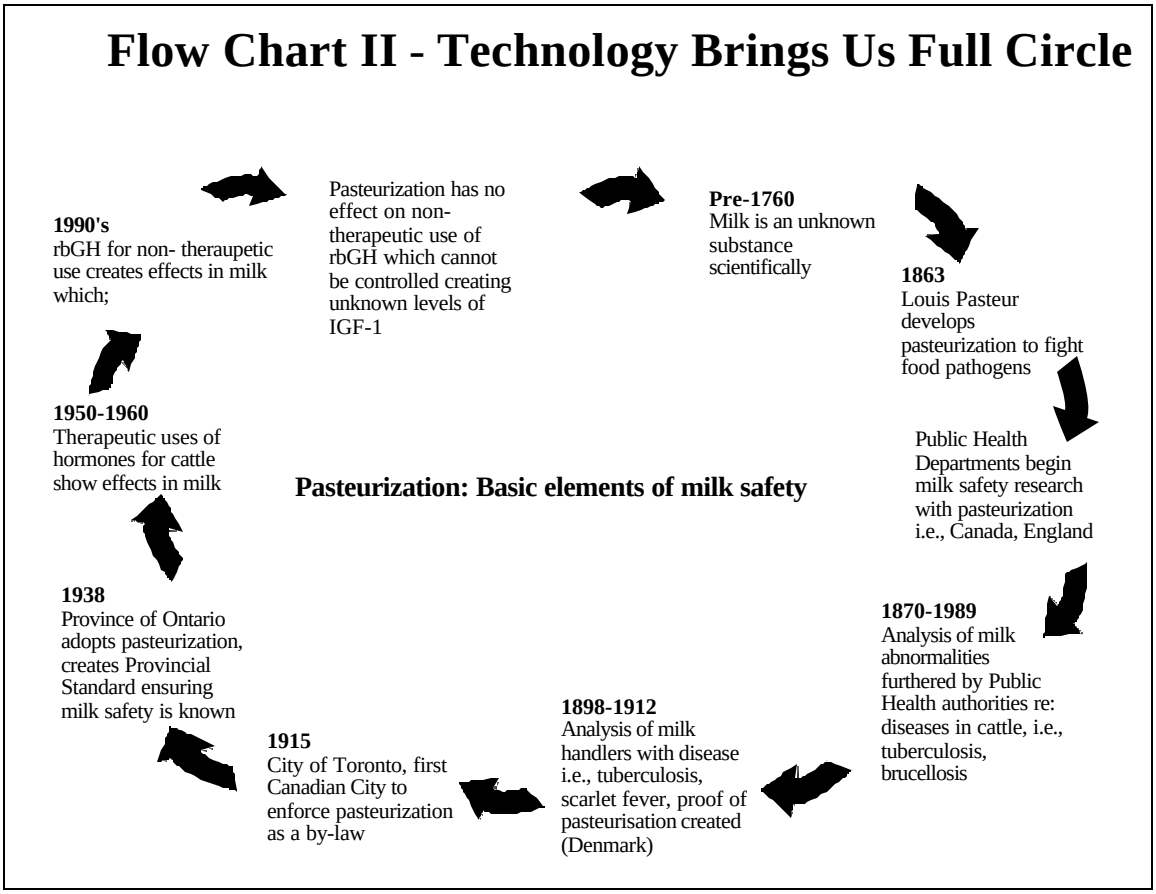
4. That all references involving rbGH be re-examined for relevance to human or animal safety in real-life situations;

5. That a new and singular definition of milk be incorporated into the National Dairy Code, Division 8 of the Food and Drugs Act, and other legislation to advance a cohesive and clear profile of milk for use in human consumption, and the type of animal deemed acceptable to produce this milk;

6. That milk from rbGH-modified cows be declared unfit for human consumption, because the adulterated animal and the biochemical properties of its lacteal secretion are not in accordance with the specifications, spirit or scientific objectives within Division 8 of the Food and Drugs Act, and because human modifications of genus *Bos* or *Taurus* lead to violations of Hazard Analysis Critical Control Point procedures, incorporated within City health units and the National Dairy Code.


Flow Chart I - Technology Brings Us Full Circle
Pre 1760
Dairy Cattle are of unknown capabilities and not identified scientifically for collaborative assessment
1760-1790
Robert Bakewell originates the protocols to study and prove breed improvement
1800
Bakewell's success creates interest in establishing scientific breed associations for identification and measuring of livestock
1830's
Importation of Registered European stock to North America
1832
Importation of Registered Dairy Stock of known parentage to Canada
1880's
First Dairy Breeders' Associations formed to scientifically evaluate identified cattle
1900
Canadian Government creates an act to recognize breed associations
1912
Animal Pedigree Act becomes federal legislation promote breed improvement (currently still enacted)
1900
Hormone Research begins
1939-1942
USDA warns of hormone use re: non-therapeutic supplementation of hormones
1960 - current
Hormones designed specifically for therapeutic use
1993
rBGH in the U.S. allowed for unscientific use by farmers on dairy cattle
Therefore
Scientific policy of sustainable animal production

Flow Chart II - Technology Brings Us Full Circle



GENERAL INTRODUCTION

Recombinant bovine Growth Hormone (rbGH) is an injectable synthetic hormone designed to override the inherent physiology of a dairy cow, modifying her metabolism to produce more milk.

Health Canada's 1999 decision to reject rbGH for use in Canada was limited, incomplete and inconclusive. The decision was made strictly on the grounds that rbGH posed a health risk to cows. Health Canada regulators accepted arguments that rbGH posed no known risks to human health. As a result, it is still possible for Canadians to drink rbGH milk when they buy milk or milk products exported from the U.S., where rbGH is legal. Because the grounds for Health Canada's decision were so narrow, there are many ways to get around it. Only one brand or variant of rbGH was denied a license. Other variants may still be proposed and approved. The manufacturer of the drug rejected by Health Canada still enjoys the right to appeal the decision. Nor does Health Canada's decision prohibit future attempts to extrinsically modify dairy cattle or feeds through genetic engineering. TFPC presents our fifth report on rbGH to expose the deficiencies of the review process that led to such worrisome results.

To describe rbGH as contentious would be an understatement. The debate is characterized by the following polarized positions:

Table 1

Proponents claim rbGH	Opponents claim rbGH
Is safe for use on dairy cows	Is not safe for use in dairy cows
Is beneficial to dairy farmers	Is harmful to dairy farmers
Milk from rbGH injected cows is safe because expert committees say so due to the evidence	Milk from rbGH injected cows is a risk according to independent scientists' review
The United States Food and Drug Administration properly evaluated this drug	The European Union says the drug was not properly evaluated in the United States

The rbGH debate has grave implications for public health nutritionists who promote milk and milk products. It raises a public question of whom to trust regarding the health and safety of milk.

The debate outlined in Table I needs to be situated within the known and uncontroversial cardinal requisites of a progressive dairy industry, which Canada and Ontario have enacted under legislated mandates for public health departments, processors and dairy farmers. The standards in the Canadian dairy industry rest on three premises:

1. Dairy cattle with known characteristics are the foundation of a stable milk supply;
2. Milk is a product of known characteristics;
3. Raw milk is handled and processed with known and proven procedures.

In examining rbGH research as it relates to the above, we find that:

> **rbGH research fails to meet legislated expectations of drug review, pasteurization or dairy animal evaluation, and the corresponding public health agenda promoting milk as a known and safe substance,**
>
> and;
>
> **rbGH research fails to acknowledge standards developed within federal and provincial legislation, codes and guidelines which make it clear that any indiscriminate hormone use in dairy cattle is unacceptable.**

Health Canada's refusal to license one brand of rbGH does not resolve concerns around contraventions of cardinal dairy industry requisites by rbGH research protocols. Research was deficient in the following ways:

1. There was no standard toxicological data package, in contravention of the standard procedures in drug review;

2. There was no accounting for precise effects of pasteurization;

3. There was no accounting for proof of pasteurization protocols, using the official MFO-3 method to determine Phosphotase Activity in Dairy Products;

4. There was no accounting for provincial milk, cattle and pasteurization laws;

5. There was no accounting for the Animal Pedigree Act for registered livestock;

6. There was no accounting for milk recording rules and regulations; and

7. There was no accounting for established animal health principles banning "overstocking," a practice inducing stress in the dairy cow, specifically the udder (mammary) and the rumen (stomach), by forcing more milk into the udder and gorging the rumen. This is considered unethical, a cause of mastitis and digestive disorders, and a negative influence on established milk quality standards.

These shortcomings occurred despite prophetic warnings by the United States Department of Agriculture (1942), and failures with earlier hormones such as thyroxine and oxytocin (Coles, 1962), used in long-term supplementation.

This neglect of basic procedures followed from a failure to recognize the bio-chemical profile of raw milk, and the animal providing said lacteal secretion, as required in Division 8 of the consolidated regulations of the Food and Drugs Act. The key regulation states:

> **Milk shall be the normal lacteal secretion obtained from the mammary gland of the cow, genus *Bos*.**

What seems to be happening here is a classic case of "regulatory drift." Without regard to the law, or first principles, regulators and farmers have tolerated an increased use of hormones. At first, they were allowed for specific therapeutic purposes, for estrus or conception problems in a cow, for instance. Next, they were allowed for programming cows to estrus artificially. Then came a proposal to use synthetic hormones for production, not therapeutic, purposes. Such drift and devolution are fraught with potential for danger and irresponsibility, and compromise the entire network of dairy regulations. Once drift sets in, no-one has responsibility for either permitting or prohibiting controversial practices.

The toleration of undisciplined hormone use by regulatory bodies created anomalies which undermine public confidence and safety. We are issuing this discussion paper to achieve the following:

1. to encourage the public and regulators to respect the cardinal requisites of the Canadian dairy industry relating to raw milk as a known substance, and to bolster the standing of tested public health traditions;

2. to reaffirm the fundamental requisites by highlighting the precedents within the regulatory structure that are scientifically designed to ensure public health and a progressive dairy industry;

3. to reassess rbGH research and application protocols against the benchmarks of these cardinal requisites;

4. to start rebuilding the policy structure so that the shortcomings revealed during the review of rbGH are not repeated.

In reviewing laws, there are two important things to consider: the definitions of words within legislation; and the way points are clarified by other statutes. For example, an act may incorporate a particular word in its definitions, referring to the location of the detailed definition in another statute. Legislators must take great care to co-ordinate meanings in legislation to prevent loopholes, vague interpretation or contradiction.

The key statutes, codes, by- laws and regulations bearing on milk, milk processing and cattle are listed in Table 2.

Table 2		
Federal	**Provincial (Ontario)**	**Non-Governmental Groups**
Consolidated Regulations of the Food and Drugs Act	Health Protection and Promotion Act	By-laws of Dairy Cattle Breed Associations
National Dairy Code	Milk Act	Canadian Milk Recording Board Regulations
Animal Pedigree Act	Artificial Insemination Act	

We have found that the regulations and statutes have been interpreted too loosely over the years. Some interpretations have been so loose that they contradict the original objectives of lawmakers. This is an issue in its own right, over and above deficiencies in Health Canada's regulatory review of rbGH. Patterns of legal and scientific continuity established over a hundred years are at risk.

During the time of rbGH research, the collaborative agreements made by Canadian dairy farmers recognized that the indiscriminate use of any hormone is detrimental to the integrity of three fundamentals for evaluation:

1. genus *Bos*, cattle;
2. raw milk from genus *Bos*;
3. the genealogical database (herd-books) of registered cattle, which constitute scientific evidence.

Had these fundamentals been taken into account, the entire controversy around rbGH would never have occurred. Ironically, this technology, promoted as a progressive management tool for farmers, could lead to the demise of the dairy industry. This technology could unwittingly return the dairy industry to its original state, before cattle were scientifically identified, and before milk was a known substance. It is said that those who refuse to learn the lessons of the past are doomed to repeat them. The haphazard regulation of rbGH is a case in point.

Section 1:

"The more that was learned about the quality of milk and cream and the methods of testing for quality, the more obvious it became that there are significant differences in milk production capability among various breeds of dairy cattle and between individual members of the same breed. Production for the market could not tolerate dairy cows which were 'boarders' – that is, cows which consumed the same amount of feed as others but which produced a lesser amount of saleable output. The closing years of the nineteenth century witnessed the establishment of herd books recording the pedigree of purebred Holstein, Ayrshire, and Jersey cattle. Dairy herd associations began to appear and these provided farmers with a means of recording, and having recorded for others to peruse, the milking capacity and butterfat production of individual cows. Scientific breeding and selection gradually became commonplace in the dairy industry." G. Church, An Unfailing Faith: A History of the Saskatchewan Dairy Industry

The First Requisite: Genus *Bos*

Without cows, there can be no cows' milk. No technology can replicate milk from a cow, and a cow does not need technology to produce milk. For this reason, protecting the heritage and standards of dairy cattle is fundamental to a continual supply of quality milk.

The federal government's definition of milk or whole milk requires cattle (genus *Bos*) to produce milk.[5] (Goats are classed under a separate section of the regulations.)

Most of today's dairy cattle are bred from original parent stock developed by English and European breed associations. These breed associations descended from the scientific commitment of Robert Bakewell (1725-1795 A.D.), founder[6] and developer of a scientific protocol called "breed improvement"[7] started in 1760 (see Appendix D). Bakewell's successes in breeding, and proving he had bred, better livestock aroused interest in improving livestock in England. This was achieved by keeping carcasses and skeletons to show variations between generations in the breeds he was

[5] Consolidated Regulations of the Food and Drugs Act, Division 8, sect. B.08.003(s), 1995

[6] The Complete Grazier and Farmer's and Cattle Breeders Assistant, A compendium of Husbandry, originally written by W. Youatt, Member of the Council of the Royal Agricultural Society of England, Thirteenth Edition, by W. Fream, University of Edinburgh , page 17, 1893, - See also - Boys' and Girls' Calf Clubs, Members Handbook, printed by the direction of the Hon. James G. Gardiner, Minister of Agriculture, Ottawa, 1946, also see The Use of Drugs in Food Animals, Benefits and Risks, National Research Council, page 49, 1999

[7] Ibid, see also, Harmsworth's Universal Encyclopedia, J.A. Hamerton, page 847, circa 1920

improving.[8] The goal was to identify cattle which could healthily provide the most product on the least amount of feed, be reproductively sound, and have the necessary physical traits to withstand the environment and production demands of the livestock industry.

To achieve a scientific distinction of "improvement," animals have to be identified and registered. The importance of this 240 year-old experiment is still protected by a Canadian law known as the Animal Pedigree Act. Its mandate is to promote breed improvement and authorize breed associations to prove breeding value of livestock.

Three fundamentals prove breeding value among dairy livestock. The first is sound reproductive capability, evidence that a bull produces viable semen and a cow can give birth to a newborn within an approximate one-year span. The second is physical conformation of a cow that can withstand milk production and the environment the animal is exposed to. The third is the milk record of a dairy female animal, evidence to show not only profitability for the farmer, but also to provide a direction for genetic improvement. Concern for these fundamentals is exemplified by the following prohibitions set out under Canadian Milk Recording Standards:

1.1.6.1 Any action by a person who, by an act or voluntary omission, knowingly and with intent to mislead, impairs or attempts to impair the reliability of any information about an animal or herd.

1.1.6.2 Any practice or the administration of a product (stimulant, drug, Oxytocin), to an animal during test day. This rule does not forbid proper medical attendance on an animal at any time.

1.1.6.3 Any practice that is intended to create an abnormal yield of milk or components in the milk.[9]

The earliest milk register in England was created out of a need for greater exactitude in the dairy sector.[10] Milk recording came to Canada out of the need to develop credibility of the early breed associations. The Holstein-Friesian Association of Canada (now Holstein Canada) instituted the Record of Merit Program (ROM) in 1901[11], and the Dominion Department of Agriculture instituted the Record of Performance program (ROP) in 1905[12]. (This program was cancelled by the federal government in the early 1980's, and delegated to provincial milk recording associations). These programs create proof of breeding value, which leads to breed improvement.

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[8] Harmsworth's Universal Encyclopedia, J.A. Hammerton, page 847, circa 1920

[9] Canadian Milk Recording Standards, 1992. Note: now repealed.

[10] The Complete Grazier, Youatt, Fream, 1893, page 245.

[11] History of the Holstein-Friesian Breed in Canada, G.E. Reaman, 1946, pg. 2

[12] Ibid

Breed improvement is a purpose set out in section 3a of the federal law known as the *Animal Pedigree Act*,[13] enacted by Parliament in 1912. It sets out the legislated mandate for breed associations, as well as the obligations of any Canadian citizen who chooses to become a breed association member. It legally binds[14] all members of a breed association to obey the by-laws established by their association. It is under the jurisdiction of the Department of Agriculture and Agri-Food.[15] This law upheld the stringent regulatory process followed by Canadian breed associations since the 1880's. The stellar role and exemplary work of these associations were recognized in 1900, with the enactment of the *Dominion Act for the Incorporation of Livestock Associations.*

All pedigrees or certificates of registration of dairy cattle still have permanent registration numbers for individual animals on them. The basic information on a legal pedigree is the name of the animal, a registration number, the name of the sire (father) with his registration number, and the name of the dam (mother) with her registration number, date of birth, breeder and/or owner. Today, the original pioneer herd books or databases are maintained by each generation of breeders, with continual updates of each generation of animals since the late 1800's. This record-keeping system is reflected within the definitions of the *Animal Pedigree Act*, which defines "foundation stock" in relation to a distinct breed. It means such animals are recognized by the Minister of Agriculture and Agri-Food as constituting the breed's original stock, from which all purebred and registered livestock descend.

No-one has rescinded any by-law of any dairy breed association supporting breed improvement or maintaining the genealogical database of respective breeds; nor has the purpose of the Animal Pedigree Act ever been altered or revised. Therefore, no legally-registered animal can have its inherent physiology supplemented or altered by any externally administered hormone; otherwise, the credibility of any study establishing an animal's breeding value is negated.

The indiscriminate use of any hormone in any registered animal contravenes the Animal Pedigree Act, and opens the doors to deregulation and scientific fraud. An unpublished report by the Law and Government Division of the Library of Parliament assessing the implications of rbGH for the Animal Pedigree Act gives grounds for careful consideration of this matter[16].

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[13] The Animal Pedigree Act, Queen Elizabeth II, Chapter 13, Assented May 25th, 1988, now expressed as Chapter 8, (4th supplement) Revised Statutes of Canada, 1985, with amendments expressed in Canada Statute Citator, A5-5, December, 1995, and the Consolidated Statutes of Canada, updated to April 30, 1998

[14] Ibid, sect. 17

[15] Remembering also that breed improvement and Bakewell was recognized by prior federal department of agriculture ministers, i.e. James Gardiner (1946), and provincially, Duncan Marshall, Alberta, (1909-21)

[16] Recombinant Bovine Somatotropin and the Animal Pedigree Act, G. Lafrenier, Jan. 12th, 1995. Although the report is well-done, it leaves several incorrect impressions that flow from inadaquate understanding of scientific requirements within dairy law and policy.

All genealogical profiles of all registered dairy animals emanate from programs which incorporate an identifying milk recording number for every cow in dairy herds on milk recording programs. These numbers are correlated to that animal's registration number within breed association herd-books or databases. (See bibliography, for an example of herd book registration number sequences). These identification numbers serve as scientific evidence for breeders, establishing baselines to establish proof of breeding value. As the introduction to the first volume of milk recording released by the Holstein-Friesian Association of Canada puts it:

> *The classification of record cows under their sires and under their dams affords invaluable information regarding the families which are uniformly great producers and cannot help but prove of great assistance to all scientific breeders.* (G.W. Clemons,1912[17])

Nearly all dairy farmers in Canada use registered sires with recorded genealogical backgrounds. In 1967, Dairy Farmers of Canada sponsored the first Canadian Conference on Milk Recording.[18] That conference defined milk recording as follows:

> *Embracing all of those practices and programs which are relevant to the accumulation and the utilization of data on milk recording and the analysis of milk constituents. Such data may be utilized for several purposes such as milk management and breeding within herds, substantiating the value of livestock offered for sale and sires used artificially.*

Not all dairy farmers in Canada are members of a dairy breed association, of which there are eight.[19] However, a vast majority (75%) of dairy farmers propagate their herds by using artificial insemination.[20] Most of the remaining dairy farmers still use natural service on their cows by a bull (sire). All bulls within artificial insemination studs are registered within the Canadian or foreign herd-books or computer databases. In order to select the worthiness of a sire for use, all daughters must be evaluated for milk production, base constituents of milk (fat and protein) and milk quality (somatic cell counts). Also included is the type conformation ! or how taxoconomically correct the body structure of daughters of a registered sire are ! in comparison to a standard defined by a breed association.

The supplementation of any dose of natural pituitary derived bovine Growth Hormone (pbGH), or rbGH,

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[17] Canadian Holstein-Friesian Yearbook, Volume 1, 1912 containing a list of all official and semi-official butter and milk records of the Holstein-Friesian Association of Canada as admitted to the Record of Merit and Record of Performance.

[18] Canada's Holsteins, P. Lewington, page 195, 1983.

[19] These associations represent the following recognized breeds under the Animal Pedigree Act, Holstein, Ayrshire, Jersey, Guernsey, Milking Shorthorn, Brown Swiss, Canadienne, Dexter.

[20] Canadian Dairy Network Statistics, Jersey Breeder Journal, March 1996.

drugs or stimulants which create abnormal milk production, obscures the reliability of information on an identified and/or registered dairy animal. The animal producing the milk is not the one registered at birth. She has been modified beyond her inherent capabilities, (see Tables 9 and 10, Appendix E) This is clearly a violation of milk recording standards.

Credibility and validity of records are stated objectives of all dairy farmers. They require identified cattle for recording to be evaluated to prove breeding value. This benefits not only dairy farmers, but the public as well, since it constitutes a basis for food security. Given this, why was rbGH, a drug designed to stimulate milk production in a cow beyond her inherent physiological capabilities in the environment she is exposed to, considered for use?

Evaluation of rbGH was complicated and confounded by the drift toward official tolerance of hormones, as listed in Table 3, to solve breeding problems in dairy cows. The therapeutic use of hormones on dairy farms for over 40 years has clouded an objective assessment of rbGH, by failing to highlight principal differences between the application of these hormones and the application of rbGH, and thereby permitting regulatory drift to establish itself. Traditional hormones are designed for therapeutic use with animals under stress. Use is restricted within controlled parameters, and withdrawals for milk and meat are specified. Nevertheless, we have found this regulatory drift to be a key oversight. These hormones may have been well-intended, but over the long-term they led to the masking of deficient dairy cattle incapable of fully functioning under production or environmental stress.

"Stress" is key to the rbGH issue. The National Institute of Health,[21] in its assessment of rbGH, listed key research areas, one of which was "define stress on a cow." No response seems to have been given to this request. In the absence of official response, we suggest that stress in cattle be defined (Miller, et al 1967, Blood, et al 1960) as any condition that would psychologically or physiologically disrupt a cow's behavior, sense of well-being, or metabolism. For example, a new environment can stress an animal. So can hot weather, illness, parturition, or over-crowding. In the literature, the case is made that animals' minds or thoughts, though far dimmer and simpler than humans, are subject to a a conceptual equivalent of human stresses.[22] Ensminger,[23] who wrote several texts on cattle, included "psychological tension or strain" within his definition of stress.

Dairy literature describes heavy milk production as stress. Reproductive problems are linked to that stress. Bailey 1980, makes the case that production and reproduction are closely related, and that a hormonal balance that permits heavy milk production may act at the same time to prevent estrus in

[21] National Institutes of Health Technology Assessment Conference Statement- Bovine Somatotropin, Dec.5-7, 1990, page 15.

[22] Black's Veterinary Dictionary, W.C. Miller, G. P. West, Eighth Edition, page 883, 1967, see also Veterinary Medicine, D.C. Blood, J. A. Henderson, page 43, 1960.

[23] Dairy Cattle Science, M. E. Ensminger, Second Edition, page 326, 1980.

dairy cows.[24] Ensminger states that high-producing dairy cows are constantly under stress. This point is accepted in many reviews of rbGH, such as Burton, et al, 1984[25] and Zinn,1996.[26]

Stress during milk production has been in evidence since records were kept to measure breeding value of livestock. In order to improve milk production genetically, assessment of stress in relationship to reproductive performance is necessary. The first scientific livestock breeders, lacking the technology to mask stressed dairy cattle in their herds, eliminated genetically-defective stock which could not reproduce another generation. This caused short-term pain, but farmers were rewarded with calves from cattle genetically able to produce higher amounts of milk and get pregnant in the same environment. This created long-term gain.

By contrast, incorporating therapeutic hormones to re-establish estrus in stressed dairy cows allows defective cattle to be masked, perpetuating a new generation of inferior livestock. The therapeutic use of reproductive hormones creates a scientific illusion. As mentioned earlier, milk records are not only important to establish the volume of milk a cow can produce within a given environment, but also the consistency of lactations in a dairy cow's lifespan. This consistency provides proof of reproductive soundness, a requirement of proving breeding value.

[24] Veterinary Handbook for Cattlemen, J.W. Bailey, D.V.M. Fifth Edition, revised I. S. Rosoff, page 167, 1980.

[25] Burton, J.L. McBride, B.W., Block, E., Glimm, D.R., Kennelly, J.J., a review of bovine growth hormone, Journal of Dairy Science, vol. 71, 167-201. 1994.

[26] S.A. Zinn, B.Bravo-Ureta, The effect of bovine somatotropin on dairy production, cow health and economics, Progress in Dairy Science, ISBN, 0 85198 974 8, pages 59-85, 1996.

As an example, see the following table. Cow A calves each year for five years, and shows sound reproductive consistency (desirable) in comparison to Cow B (undesirable).

Cow A			
age at calving		**milk kg.**	**fat kg.**
years	**days**		
2	00	6,700	254
3	10	8,000	321
4	40	8,897	366
5	22	10,000	400
6	00	9,965	397
Cow B			
2	100	6,700	254
4	00	8,000	321
5	320	8,897	366

Cow B was proven to be unsound reproductively, because she genetically could not handle the stress of production within her environment, as shown by the inconsistency of the age at calving. This sequence, prior to the introduction of reproductive hormones, serves as evidence of unsound breeding from a reproductive point of view. However, with hormone use, Cow B can emulate the consistency of the sequence of lactations of Cow A, creating a scientific illusion of reproductive soundness. This undermines genetic stability, a stated objective of the dairy industry. This type of situation has stood in the way of objective assessment of rbGH by farmers themselves, as well as regulators. Farmers sometimes make decisions geared to individual animals and to their own short-term objectives. This undermines the long-term and collective structures that have historically safeguarded milk safety and dairy industry sustainability. It is a threat to food security because it undermines scientific knowledge required to maintain genetic stability.

For over a century, breeders and breeders' associations worked from the premise that quality milk and a sustainable dairy industry derive from dairy cattle with known inherited characteristics. For over a century, laws governing animal pedigree and proof of breeding honoured this tenet of a progressive dairy industry. This tradition has been compromised over the past 40 years by a permissive approach to therapeutic hormones. The tradition was almost overturned, without hindsight or forethought, by federal regulators who failed to define rbGH, a hormone which has no therapeutic purpose whatsoever, as a contravention of the first principle of a safe and sustainable dairy industry and milk supply.

Table 3

Hormones Allowed for Use in Canadian Dairy Cattle

Drug	Purpose or Aid	Milk Withdrawal	Meat Withdrawal
Oxytocin (5 different brands) see # below	induce milk letdown, inducing uterine contractions	#1 - 24 hours #2 - 24 hours #3 - 24 hours #4 - 24 hours #5 - 72 hours	3 days 3 days 3 days 3 days 3 days
Estrumate	causes functional and morphological regression of the corpus luteum, resulting in estrus in 4-5 days, now used for controlled breeding programs, or to induce abortion	none	48 hours
Cystorelin	treatment of cystic ovaries in dairy cattle	12 - hours	7 days
Lutalyse	induce estrus, uterine contractions,	none	2 days
Factrel	induces ovulation	12 - hours	7 days

Source: Compendium of Veterinary Products, ISBN 1-896674-14-3, Canadian Animal Health Institute, Sixth Edition, 1999

#1 Oxytocin P.V.U. Din: 00159123
#2 Oxytocin V`etoquinol Din: 00052124
#3 Oxytocin Injection -Ayerst Din: 00713201
#4 Oxytocin Injection - Bimeda-MT Din: 00141828
#5 Oxytocin Injection P.V.L. Synthetic -Double U.S.P. Strength Din: 00308277

Main purpose: Originally for therapeutic use only, specifically for milk let down (Oxytocin), or alleviating estrus problems due to stress (too much milk production, hot weather, illness). All have either milk and or meat withdrawals listed on the label or the package information insert.

Table 3 reveals the clear contradiction created by rbGH for non-therapeutic use. All the hormones in Table 3 have either milk or meat withdrawals for specific therapeutic use for only short effect. Yet rbGH for continual supplementation over 150 days in a lactation would be considered for use in the milk supply, and not be subject to any proper long-term safety studies.

Section 2:

"The first priority is to do no harm." Hippocrates

The Second Requisite: Normal Milk

Canadian law specifies that only normal milk can be sold; milk tainted by undesirable influences, adulterated milk, and milk that doesn't respond to established procedures such as pasteurization are not normal, and cannot be sold.

Before assessing rbGH, it's worth reviewing another mainstay of dairy regulation: the definition of normal milk. Hunziker[27] 1940, recognized by the Ontario Department of Agriculture as an expert on butter quality,[28] states:

> *Milk secretion is a physiological function. If this function is abnormal, the properties of the resulting product - milk - may also be, and often are, abnormal. Any condition which materially disturbs physiological functions of a cow, therefore, tends to disturb the normal chemical, physical and physiological properties of milk and its products, and jeopardizes their wholesomeness, flavour and market value.*

Research on rbGH shows that the drug disturbs the physiological function of the cow, producing an abnormal biochemical profile in milk. During the period of rbGH research and review, from 1975 to 1999, milk was defined within Division 8 of the Consolidated Regulations of the Federal Food Drugs Act, which governs Health Canada, as follows:

Section B.08.003.(S) Milk or Whole Milk

(a) shall be the normal lacteal secretion obtained from the mammary gland of the cow genus *Bos*; and

(b) shall contain added vitamin D in such an amount that a reasonable daily intake of milk contains not less than 300 International Units and not more than 400 International Units of vitamin D.[29]

[27] The Butter Industry, Prepared for Factory, School and Laboratory, 3rd Edition, O.F. Hunziker, pgs. 143-144, 1940

[28] Annual Report of the Department of Agriculture, Ontario, page 117, 1931

[29] In 1975 the words " free from colostrum" were included in the definition in clause (a) but were removed in 1995. Division 8, Dairy Products, The Consolidated Regulations of the Food and Drug Act, Library of Parliament, received via member of parliament Judy Wasylycia-Leis, member for Winnipeg North, April 15, 1999

The standardization of raw milk which led to this regulation dates back nearly 200 years. Concern over bad taste or texture and a clear distaste for "tainted" milk led to early demands for regulated requirements.

The earliest scholarly considerations of tainted milk properties were developed by Fream[30] 1893. He outlined preventive measures to avoid milk tainted by exposure to unclean areas with no air ventilation, unclean vessels of containment, and feeds which created undesirable odours in milk. The earliest Canadian regulatory reference, the Milk Industry Act of 1914,[31] respects and reflects that commitment to standardize raw milk. Several prohibitions are listed in Section 4 of that Act:

> *Milk diluted with water or in any way adulterated, skimmed milk, milk to which has been added any cream or foreign fat or any colouring matter, preservative or other chemical substance of any kind; milk from strippings (the first few drawings of milk from a cow's udder); milk from a cow that is diseased.*

A further understanding of normal milk was advanced by Dean 1920,[32] who argued that milk rich with colostrum ! the sticky, sweet yellow fluid produced to feed newborn calves or after a fresh lactation !should not be fed to humans. Since colostrum contains a high percentage of albumen, which takes the place of casein in normal milk, Dean argued that the first nine milkings after a cow had calved, or the early milkings after freshening, should not be drunk by humans. Dean's judgements still stand. Eighty years later, the Ontario Milk Act[33] still stipulates the time frame to allow colostrum to dissipate before milk from a last line animal who has just calved can be pooled with normal milk.

[30] The Complete Grazier, and Farmer's and Cattle Breeders Assistant, A Compendium of Husbandry, W.Youatt, Esq. Member of the Royal Agricultural Society of England, 13th edition, revised by W. Fream, , University of Edinburgh, pgs. 302 to 305, 1893

[31] The Dairy Industry Act, 1914, (Chapter 7) and Regulations, Bulletin No. 42, Dairy and Cold Storage Series, published at the direction of the Hon. Martin Burrell, Minister of Agriculture, June, 1914, by J.A. Ruddick, Dairy and Cold Storage Commissioner

[32] Canadian Dairying, 5th edition, Henry H. Dean, Professor of Animal Husbandry, University of Guelph, 1920, pp 49-50.

[33] Office Consolidation, Milk Act, Revised Statutes of Ontario, 1990, Chapter M.12, as amended by: 1991, Chapter 53, s.2; 1994, Chapter 27, s. 30; 1996, Chapter 1, Sched. M, s. 70, 1996, Chapter 17, Sched. H, Jan. 1997, regulation 761, sect. 5 (1) (a) (i), pg. R9.2

Eckles et al 1943, expands the definition of milk as the normal secretion of the mammary glands of mammals,[34] and extend the prohibited practices in the 1914 Dairy Industry Act. This expansion of "normal" deals with the specific biochemistry of milk from dairy cows, and with the causes of abnormal tastes and odours in what is referred to as "tainted" milk. In this study, tainting can have one of six sources.

1. It can come from the cow herself; if she is in a disturbed physical condition, substances giving objectionable taste are secreted in the milk.

2. It can come from the cow's feed, which imparts odours or flavours that are taken in by the blood and secreted in milk.

3. It can come from pronounced odours to which milk is exposed, the severe barn smell from manure, for instance.

4. It can come from decomposition of milk constituents resulting from the growth of bacteria and other micro-organisms.

5. It can come from foreign material in milk.

6. It can come from changes due to chemical action.

Normal milk principles based on improved technologies were presented by Sommer[35] 1946. He established that more stringent protocols were needed to establish bio-chemical influences in milk by understanding the normal chemical profile of a dairy cow in a lactation and changes within the environment, feed, age, etc. Coles et al 1962, carried on the direction of restricting the definition of normal milk.[36] Milk affected by udder disease or similar trauma did not qualify as normal, according to these scholars.

These enduring standpoints allow for a scientific and objective understanding of milk properties, based on both the genus *Bos* and the environment the cow is exposed to. Technically, both are control points in an ongoing experiment. Regulations regarding the type of mammal, the environment this mammal should be exposed to, and the precautions required to avoid spoiling raw milk, ensured both marketability and public safety.

[34] Milk and Milk Products, C.H. Eckles, W.B., Combs, H. Macy, 3rd Edition, pgs. 63-64, 1943

[35] Market Milk and Related Products, H.H Sommer, Professor of Dairy Industry, University of Wisconsin, pgs. 124-210, 1946

[36] Introduction to Livestock Production Including Dairy and Poultry, H.H. Cole, pgs. 53-54, 1962

Contemporary regulations for milk producers maintain this tradition. Ontario's Milk Act[37] clearly explains what constitutes unmarketable milk. Sections 3 to 11 of Regulation 761 within the Ontario Milk Act are based on prior works that helped establish the parameters of normal milk. Likewise, the word "normal" is still applied in the National Dairy Code (1997):

> "milk" means a normal lacteal secretion obtained from the mammary gland of a dairy animal; referring to cows, sheep, goats and other such species.[38]

Given this heritage, precedent demands that Canadian regulators pose this question:

> **Is the milk from rbGH-modified dairy animals normal, when compared to the milk from dairy animals not influenced by the drug?**

The answer is no, for two reasons:

1. A dairy cow, as defined under the regulations set out in Section 1, is to be the result of breeding (male x female); so the use of a non-therapeutic hormone to override the inherent physiology of a dairy animal for the purpose of milk or meat production is not recognized within Canadian law;
2. the normal biochemical profile of milk is already established by and for scientific evaluation of the genetic ranges of genus *Bos*/*Taurus*, which rbGH-modified dairy cattle cannot emulate. Research on rbGH shows severe hormonal elevations, of both Insulin Like Growth Factor-1 (IGF-1)in milk and thyroxine-5-monodeiodinase in the mammary tissue of cows.[39]

Promoters of rbGH, and even some evaluators,[40] have tried to dismiss the importance of elevated levels of IGF-1 and thyroxine-5-monodeiodinase. It's claimed that the elevated levels are within the normal range of milk from dairy cows. It's also claimed that elevated levels on rbGH cow's milk are within the normal range of human breastmilk, and consequently no riskier than human breastmilk. Critics of rbGH,

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[37] Office Consolidation Milk Act, Revised Statutes of Ontario, 1990, Chapter M.12, as amended by: 1991, Chapter 53, s.2; 1994, Chapter 27, s.30; 1996, Chapter 1, Sched. M, s.70; 1996, Chapter 17, Sched. H. and the Regulations thereunder (as amended), January 17, 1997.

[38] National Dairy Regulation and Code, First Edition Production and Processing Regulations, Canadian Food Inspection System Implementation Group. Oct. 1997

[39] Capuco, A.V., Keys, J.E., Smith, J.J., Somatotropin increases thyroxine-5-monodeiodinase activity in lactating mammary tissue of the cow, Journal of Endocrinology, vol. 121, 205-211, 1988, See also, Burton, J.L. McBride, B.W., Block, E., Glimm, D.R., Kennelly, J.J., a review of bovine growth hormone, Journal of Dairy Science, vol. 71, 167-201.1994

[40] Correspondence from Dr. M.S. Yong, Health Canada, Oct. 21, 1997, also the Joint Expert Committee on Food Additives, Fiftieth Report, 1998

on the other hand, identify abnormally elevated levels of IGF-1 as a cancer risk. Neither party to this debate has yet documented what levels of IGF-1 are safe or unsafe, which renders both arguments speculative at this point in time. (See Section 6, Part B, for a more definite approach.)

More to the point, neither party to the debate acknowledges that the debate can never be resolved in real-life conditions. This is the fatal flaw of all rbGH research to date; no-one knows how it will be used and consequently what impact it will have on cows or milk. No-one can measure or control the farmers' use of the drug once licensed, until an official test for rbGH is developed. The pooling of rbGH milk and normal milk creates a constantly fluctuating field of IGF-1 levels. These fluctuations would range from mild to severe, depending on the random decisions of individual farmers, not scientific rationale. A laboratory experiment with controls proving or disproving effects on humans would be useless and misleading without a transferable control mechanism on dairy farms.

Until tests show otherwise, present standards of "normal" should prevail. When it comes to consideration of human safety, research on both rbGH and pituitary derived (natural) bovine Growth Hormone (pbGH) confirms that the enhanced metabolic rate of a modified dairy cow cannot produce normal raw milk within the parameters of Canadian law. RbGH lacks therapeutic benefit for dairy cattle.[41] It is a production aid,[42] solely intended to stimulate abnormal milk production.

Proponents of the drug may claim rbGH modified cow milk is safe because it's diluted when pooled with other producers' normal milk. Such a claim has no validity under the Ontario Milk Act. This law is based on measurements of a single producer's actions and a single cow's influence on pooled milk. Furthermore, this pro-rbGH argument erodes the accountability of regulatory partners such as the Medical Officers and Boards of Health and their health units, who promote dairy products as known within the Health Protection and Promotion Act of Ontario.[43] The Act obliges public health authorities to regulate milk in several situations: during inspection of restaurant, investigations of adulterated food products, and enforcement of pasteurization requirements (section 42-3), for example. All such regulations are based on a historical consensus around "normal" milk.

[41] Burton, J.L. McBride, B.W., Block, E., Glimm, D.R., Kennelly, J.J., a review of bovine growth hormone, Journal of Dairy Science, vol. 71, 167-201.1994

[42] Evaluation of Certain Veterinary Drug Residues in Food, WHO Technical Report Series 832, Fortieth report of the Joint FAO/WHO Expert Committee on Food Additives, World Health Organization, section 3.3.1, 1993

[43] Office Consolidation, Health Protection and Promotion Act, Revised Statutes of Ontario, 1990, Chapter H.7, as amended by: 1992, Chapter 32, s. 16; 1994. Chapter 26, s. 71; 1996, Chapter 2, s. 67; 1997, Chapter 15, s.5; 1997, Chapter 26, Sched.;1997, Chapter 30, Shed. D, ss. 1-16 and regulations thereunder (as amended) July 24, 1998

Over the course of time, scholars and regulators settled on a definition of "normal" milk that has protected the public well. The biochemical profile of milk is central to this consensus on what constitutes "normal" milk. There is no doubt that rbGH changes this biochemical profile of milk; some also believe it changes the biochemical profile in ways that risk human health. It is unconscionable that federal regulators ever attempted to come to a conclusion on rbGH without anchoring their deliberations to this mainstay of a regulated dairy industry.

Section 3:

"Error seems to be propagated with the velocity of light. Every obstacle disappears before it, and everywhere it is welcomed. Truth, on the contrary, is usually received with indifference, and often with doubt, mistrust or suspicion." Francois Guenon, Milch Cows: A Treatise on the Bovine Species in General, 1900.

The Third Requisite: Pasteurization

Pasteurization, a compulsory measure which has protected public health for almost a century, has purposes and protocols that were overlooked by Health Canada regulators and evaluators in their review of rbGH. For this reason, judgments to the effect that rbGH poses no human health risks are lacking in merit.

Pasteurization is a precise process which took decades to perfect as a public health tool that prevented milk-borne contagious diseases such as tuberculosis, a common scourge only a century ago. It's seldom realized, even by experts, that the use of rbGH in milk production may well subvert the pasteurization heritage.

Important studies which initially led Health Canada regulators to conclude that rbGH posed no threat to human health are based on errors which should not have been overlooked by scientists who appreciated the stellar role played by pasteurization in assuring public health. As we shall show, regulators relied on studies which drew conclusions from sub-standard pasteurization procedures that failed to incorporate the relevant temperature and time frames.

Pasteurization was first applied in Canada in 1905. In 1915, Toronto became the first Canadian city to adopt compulsory pasteurization, a tribute to the dedication of the city's Medical Officer of Health, Dr. Charles Hastings, who was alarmed by the increasing number of cases of bovine tuberculosis at the Sick Children's Hospital. In 1938, pasteurization became compulsory across Ontario.[44] [45] [46] [47] [48]

[44] Ontario Whole Milk Producers League, 1932-1966, E. H. Clarke, C.L. Brethour, a history, 1966 pages 3-4

[45] For Home and Country, The Centennial History of the Women's Institutes of Ontario, L.M. Ambrose, 1996

[46] Activists and Advocates, Toronto's Health Department- 1883-1993, Heather MacDougall, 1990, page 28

[47] Why Pasteurize Milk, H.G.Campbell, Dominion of Canada, Department of Agriculture, Pamphlet 124, -New Series, The Dairy and Cold Storage Branch, J.A. Ruddick, Commissioner , Published by direction of the Hon. Robert Weir, Minister of Agriculture, page 4, 1930

[48] Ontario Whole Milk Producers League, 1932-1966, E. H. Clarke, C.L. Brethour, a history, 1966 pages 3-4

As a result of its effectiveness ever since, pasteurization is often taken for granted. Few people today appreciate the 70 years of scientific work that went into making pasteurization so reliable.

Pasteurization honours the eminent nineteenth century French scientist, Louis Pasteur.[49] Pasteur discovered that fermentation is the result of living bacteria, which have parents and which themselves reproduce. He further discovered that bacteria can be destroyed with heat as low as 140 degrees Fahrenheit. By properly applying heat, it became possible to destroy undesirable bacteria without destroying species of bacteria that humans valued. Pasteur's work was focussed on wine. His ideas were applied to milk by Soxhlet, a German biochemist, in 1886.[50] Denmark instituted compulsory pasteurization in 1898[51] in an effort to limit the spread of tubercular disease.[52]

Ensuring public confidence was of the utmost importance for Danish authorities, so a test was developed to prove milk was actually pasteurized. This test effectively ended any misrepresentation by unscrupulous milk dealers.[53] This test noted evidence of a milk format known as perioxidase.[54] Newer tests furthering the public trust are still required by Ontario[55] and by federal Food and Drugs regulations.[56] The newer official method, currently known as "MFO-3, Determination of Phosphotase Activity in Dairy Products," requires the reduction of the milk enzyme known as alkaline phosphotase to the tolerances listed within the official method.

Until 1926, regulators had a hard time coming up with precise standards and clear data that made these standards credible. Some pathogens in cattle had varying tolerances to heat, for instance. (See Table 4). A lot of trial and error and rigorous follow-up went into the development of logarithmic scale systems (heat vs time) underlying modern standards now incorporated within provincial laws across Canada. Such standards,

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[49] The Butter Industry, Prepared for Factory, School and Laboratory, 3rd Edition, O.F. Hunziker, page 260, 1940

[50] Milk and its relation to public health. In Ravenel, Mazyck, P., ed. A Half Century of Public Health, New York, American Public Health Association, 236-289

[51] Milk and it Hygienic Relations, Janet E. Clayton, Assistant Medical Inspector under the Local Government Board, Published under the direction of the Medical Research Committee, London England, page 65, 1916

[52] Ibid, see also Milk and Milk Products, C. H. Eckles, W.B, Combs, H. Macy, 3rd Edition, pgs. 176-177 1943

[53] Loc cit.

[54] See footnote 51.

[55] Office Consolidated Health Protection and Promotion Act, Revised Status of Ontario, 1990, Chapter H.7, as amended by 1992, Chapter 32, s. 16; 1994. Chapter 26, s. 71; 1996, Chapter 2, s. 67; 1997, Chapter 15, s.5; 1997, Chapter 26, Sched.; 1997, Chapter 30, Sched. D, ss. 1-16 and regulations t hereunder (as amended) July 24, 1998, see section 43 (1), (2)

[56] Consolidated Regulations of the Food and Drugs Act, Division 8, Section, B.08.002.2 received by correspondence May, 1999

and the demanding, complex and comprehensive research behind them, cannot be waived or dismissed lightly. It's reasonable that new technologies and drugs influencing milking dairy cattle should conform to measures of pasteurization, a proven public health safeguard, not the other way around.

Table 4

Early Pasteurization capabilities

	Temperature	Time heated
Boiling point of water	212 degrees F.	
Pasteurizing temperature	145 degrees F.	30 minutes -quickly cooled to below 50 degrees F.
Tuberculosis bacteria killed at	139 degrees F.	30 minutes
Typhoid bacteria killed at	137 degrees F.	30 minutes
Diphtheria bacteria killed at	131 degrees F.	30 minutes

Source: footnote[57]

Though many of the disease risks once associated with milk have been all-but-eliminated by modern safety measures, a clear and precise vigil around pasteurization remains the order of the day. The same qualities that give milk its vitality render milk prone to spoilage and contamination by pathogens. The most minor slip in protocols for maintaining milk safety could lead to the re-emergence of diseases such as tuberculosis or brucellosis.

Had Health Canada officials been more aware of the science around pasteurization, they would have taken more care before accepting the judgments of the U.S. Food and Drug Administration and the Expert Human Safety Panel appointed by Health Canada. These bodies deemed it unnecessary to collect human chronic safety data on rbGH. They came to this recommendation based on substandard references. As it happens, a crucial reference was based on the wrong temperature\time frame for pasteurization and failed to establish objectively that the milk samples from cows injected with rbGH were actually pasteurized.

As well, evaluators maintained that elevated levels of Insulin-Like Growth Factor-1 in milk from rbGH modified dairy cows would be denatured by infant formula pasteurization process, which is 250 degrees F. for 20 minutes. This temperature/time frame is not the relevant temperature/time frame for fluid milk consumption. Consequently, there is no legitimate evidence that IGF-1 is denatured by pasteurization as it is actually practised in commercial processing.

[57] A note on the home pasteurization of milk, Dr. G E Hood, Chief, Division of Dairy Research, page 7 Why Pasteurize Milk, H.G.Campbell, Dominion of Canada, Department of Agriculture, Pamphlet 124, -New Series, The Dairy and Cold Storage Branch, J.A. Ruddick, Commissioner , Published by direction of the Hon. Robert Weir, Minister of Agriculture, 1930

In effect, Health Canada's regulatory review has allowed loopholes into a once-failsafe system of standards. This lack of rigour might well encourage future sub-standard procedures by companies introducing technologies influencing dairy cattle.

The key research paper for the pro-rbGH position was published in *Science*[58] by J.C. Juskevich, formerly of the United States Food and Drug Administration, and C.G.Guyer, then employed with the FDA. The report, published (contrary to FDA tradition) before the FDA made its decision public, dealt with the milk hormones rbGH and IGF-1. The authors concluded that there was no need to pursue more definitive studies because:

1. 85-90% of rbGH would be destroyed following milk pasteurization (footnoted with the wrong reference, Moore, when the actual reference was Groenewegen[59], et al 1989); and

2. human growth receptors do not recognize rbGH.

The influence of IGF-1 in modified dairy cow milk was not properly presented in this *Science* paper. The referencing of the Groenewegen et al 1989 experiment purported to show the 85-90% denaturing of elevated hormone levels in milk in a spiked milk sample, not an empirical sample of rbGH modified cow milk. The spiked milk sample contained the recommended dose of 500mg of rbGH(Cyanamid version, not Monsanto version), put into a milk sample of control cow milk. There is no analytical value in a spiked milk sample because there is no comparative value for rbGH injected cows' milk.

Groenewegen concedes that heat treatment tends to reduce levels of bGH in both control cows and rbGH modified cows; however, "the reduction was not significant,"[60] he claimed.

Likewise, the test on hypophysectomized male rats in Groenewegen's study, which tried to determine whether immunoreactive bGH in milk has a growth-promoting effect following oral ingestion, is of little value. The judgement that there was no harmful effect was based on a study time of 14 days. This contrasts with the 14-week study reported by the GAPS analysis team within Health Canada. That report shows an rbGH-specific immunoglobulin response in at least 20 % of the orally-treated rats.[61]

Table 5 below, summarizes the pasteurization discrepancies between studies used by regulators and actual

[58] J C. Jusckevich, C.G.Guyer, Bovine Growth Hormone: Human Food Safety Evaluation, Science, Vol. 249, pages 875-884, 1990

[59] P.P Groenewegen, B.W. McBride, J.H. Burton, T.H. Elsasser, Bioactivity of milk from bST -treated cows, Journal of Nutrition, vol. 120, pages 514-520 1989

[60] Ibid, page 517, discussion of table 3 figures within said report

[61] RbST (Nutrilac) "Gaps Analysis" Report, by rbST Internal Review Team, Health Protection Branch, Health Canada, April 21, 1998

commercial pasteurization requirements.

Table 5

Minimum Pasteurization Requirements
FDA (U.S.) Legal minimums and National Dairy Code, Schedule 1

	Vat[1]		HTST[2]		HHST[3]		UHT[4]	
	Time	**Temp.**	**Time**	**Temp.**	**Time**	**Temp.**	**Time**	**Temp.**
Fluid Milk	30 min.	145 F	15 sec.	161 F	1.0 sec.	191 F	2.0 sec.	280 F
			16 sec	(Canada)	0.5 sec.	194 F		
					0.1 sec.	201 F		
					0.05 sec.	204 F		
					0.01 sec.	212 F		

Note: Most dairy processors use High Temperature- Short Time (HTST) for fluid milk which is not comparable to rbGH research

Key RbGH Research Papers re: IGF-1

Groenewegen	Pasteurized Milk sample at 160 F	25-30 minutes
Juskevich and Guyer[62] Etherton[63] Daughday and Barbano[64]	Claim 90% of IGF-1 is destroyed by Infant Formula Pasteurization which is 250 F.	15-20 minutes

In his April 1989 paper,[65] Groenewegen tests for pasteurization by using a Safeguard Pres-vac Home and Cream Pasteurizer (Model P-3000, manufactured by the Schlueter Col, Jamesville Wis.) He stipulates in his experiment that pasteurization occurred at 69-71 degrees C for 30 minutes. This is a wrong temperature/time frame within commercial dairy processing, and should not have been included in a human safety assessment. A second paper by Groenewegen made similar errors.

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[62] J C. Jusckevich, C.G.Guyer, Bovine Growth Hormone: Human Food Safety Evaluation, Science, Vol. 249, pages 875-884, 1990

[63] T. D. Etherton, Clinical Review 21, The efficacy and safety of growth hormone of animal agriculture, Journal of Clinical Endocrinology and Metabolism, Vol. 72, number 5

[64] W. H. Daughaday, D.M. Barbano, Bovine Somatotropin Supplementation of Dairy cows, Journal of the American Medical Association, Vol. 264, No.8, Aug. 1990, pages 1003-1005

[65] P.P Groenewegen, B.W. McBride, J.H. Burton, T.H. Elsasser, Bioactivity of milk from bST -treated cows, Journal of Nutrition, vol. 120, pages 514-520

The original paper of three produced by Groenewegen was his Guelph University thesis, which had nothing to do with establishing biochemical properties in rbGH-modified cows' milk as a basis for human safety evaluation. In the April 1989 thesis paper,[71] Groenewegen tests for pasteurization by using a Safeguard Pres-vac Home and Cream Pasteurizer (Model P-3000, manufactured by the Schlueter Co., Jamesville Wis.) and stipulates that pasteurization occurred at 69-71 degrees C for 30 minutes in his experiment. This is the wrong temperature/time frame for a human safety assessment.

[71] P.P. Groenewegen, Effect of bovine somatotropin on millk hormone residues and growth character of veal calves, April 1989, submitted University of Guelph. See especially p. 18

The second paper emanating from the original student thesis, co-authored with his thesis advisors B.W. McBride, J.H. Burton and T. H. Elsasser,[72] uses the same pasteurization protocol. Within these two papers, there is no acknowledgment of regulatory pasteurization minimum requirements; nor is there is mention of the official MFO-3 method for proving the effectiveness of pasteurization.

A third paper, published in the Journal of Nutrition, (see footnote 69) fits the profile of the first paper. The only difference is the mention of USDA pasteurization protocols, which reflect the discrepancy between minimum legal pasteurization requirements and Groenewegens' experimental pasteurization protocols. MFO-3 has been required by law since 1981 under the Food and Drugs Act. Yet, within this third paper used by the Jusckevich and Guyer, there is no mention of the official MFO-3 method for proving pasteurization. This experiment has no value for human safety assessment because the protocols are sub-standard. Any reference to rbGH milk samples without the combination of the two legal requirements of law- minimum pasteurization temperatures and proof of pasteurization is not valid for a human safety assessment.

When notified of these errors, Health Canada Human Safety Division of the Bureau of Veterinary Drugs replied with references citing maximum pasteurization standards, not the minimum and full spectrum of pasteurization. TFPC's response to this and other matters relating to human health is documented in the Health Canada internal rBST GAPs Analysis Report.[73]

As a result of the rbST GAPs Analysis Report, Expert Panels on Human and Animal Safety were created. Correspondence with the Chair of the Expert Panel on Human Safety, Dr. Stuart Macleod,[74] indicated that this panel would not review any data pursuant to the regulations. The Human Safety Panel assumed that work would be done by the Expert Panel on animal safety. On the matter of IGF-1, the human safety panel was mandated to consider the potential impact on human safety, requiring consideration of models where justified by data. This committee used Groenwegen's work and a supplement or abstract[75] which shows no pasteurization temperatures or proof of pasteurization, just conclusions. The original study should have been referenced as evidence. As a result of such misleading and faulty references, the Expert Panel on Human Safety chose not to deploy population models to test the effects of hormone levels. (See Appendix B)

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[72] P.P. Groenewegen, B.W. McBride, J.H. Burton and T.H. Elsasser, Bioactivity of milk from bst-treated cows, Guelph University Research Report, OAC Publication No.89, June, 1989

[73] Rbst (Nutrilac) "GAPs Analysis Report, by rbST Internal Review Team, Health Protection Branch, Health Canada, April 21, 1998

[74] Phone conversation, with TFPC Staff Co-ordinator, Dr. Rod Macrae, Sept. 8th, 1998, and written correspondence from Dr. Stuart Macleod, Oct. 16th, 1998

[75] Miller, M.A., Hildebrandt, J.R., White, T.C., Hammond, B.G., Madsen, K.S., Collier, R.J., Determination of insulin-like growth factor-1 (IGF-1) concentrations in raw, pasteurized and heat-treated milk. Journal of Dairy Science, Vol. 72 (Suppl.1): 186-187, 1989

Concern is also warranted over the type of pasteurizing unit used to test for human safety in rbGH research. It is known that industrial pasteurizing units and laboratory or home pasteurizers give different readings on the thermal deaths of pathogens. Stabel, et al 1997[76], did a study to establish if current pasteurization protocols were effective in inactivating Mycobacterium paratuberculosis (also known as Johnes' Disease or fatal diarrhea) in raw milk from dairy cattle afflicted with the disease. Two methods of heat inactivation were applied using samples of infected milk: the Holder Test Tube Method, commonly used to determine thermal death rates for M. paratuberculosis and other bacteria; and, the Lab-Scale Pasteurizer Method, which simulates the high-temperature, short time (HTST) conditions 72 degrees Celsius for 15 seconds of an industrial pasteurizer unit. Stabel clearly shows the difference in bacterial activity emanating from the different methods: one method had no effect on the bacterium; the other inactivated the bacterium. This establishes the need to use relevant commercial equipment for a human safety study involving effects within pasteurized milk.

A credible reference using proper protocols, including tests proving pasteurization, is Klei, et al 1997.[77] This experiment, though not for human safety consideration, could have its information incorporated in a human safety or nutrition report, because the pasteurization protocols are calibrated to regulations, and proof of pasteurization is shown with accepted methodology. Had this respect for regulatory directives been applied in screening the quality of rbGH references, critical errors would have been avoided and the public's health better protected.

Pasteurization is recognized as a milestone in public health regulation. It is disturbing that regulators came to conclusions on the human safety of rbGH milk without insisting on the utmost rigour with regard to tests for the effectiveness of pasteurization. Sloppy research does dishonour to the scientists who laboured to introduce precise standards for pasteurization, and jeopardizes the milk consumers Health Canada is charged with protecting.

[76] J.R.Stabel, E. M. Steadham, C.A. Bolin, Heat inactivation of Mycobacterium paratuberculosis in raw milk: are current pasteurization conditions effective? Applied and Environmental Microbiology, vol. 63, no. 12, pages 4975-4977, Dec. 1997, National Disease Center, Agricultural Research Service, United States Department of Agriculture.

[77] L.R. Klei, J.M. Lynch, D.M. Barbano, P.A. Oltenacu, A.J. Lednor, D.K. Bandler, Dairy Foods, Influence of milking three times as day on milk quality, Journal of Dairy Science, vol. 80, no. 3, pages 427-436,

Section 4:

"There should be some concern about indirect effects produced by substances stimulated by rbGH in cattle and secreted into their milk. Mediators, such as IGF-1, are active in humans, and, because of their smaller molecular weight, could get across the gut and cause biological effects in humans. If there is a problem, this can best be determined by long-term studies of animals reared on milk from cows treated with rbGH. Such animals should be studied to see whether they have abnormal growth or a higher incidence of teratological effects (birth defects) or cancer. I don't expect to see any adverse effect or any other detectable difference from control animals; however, that's the only kind of study that would address such concerns..." Dr. J. Van Wyk, Professor Emeritus, Department of Medicine, University of North Carolina at Chapel Hall

The Fourth Requisite: Proper Toxicology Studies

To establish the safety of any drug, the law requires rigorous studies of any potential negative health impacts. Health Canada lacked the data to conduct such studies.

Health regulators are only human. Sometimes they make mistakes, and licence drugs that cause innocent people to suffer or die. Modern health regulators strive to ensure that these people did not suffer or die in vain. The standard data package required before any new drug can be evaluated is the regulatory monument we have built to those who suffered or died. It reduces the chance of fatal errors by requiring drug companies and health regulators to err on the side of caution and test for every possibility. In their review of rbGH, Health Canada's regulators did not follow the letter or the spirit of these regulations governing data packages.

When a company submits a new drug for licensing, it must produce a data package that allows regulators to assess the safety of that drug. There is some controversy as to whether data packages prepared by a company with a vested interest in the drug's licensing can be viewed as valid evidence. But there is a little controversy about the kind of scientific standards that must be met in a data package.

Studies on potential acute, sub-acute and chronic effects of a proposed drug are a must. Studies on animals should assess impacts over two generations. There should be teratology studies. Animal studies should include residue measures, so decisions can be made on when drug application should be withdrawn before the animal's milk or meat is consumed by humans. There should be High Performance Liquid Chromatography (HPLC) analysis verifying the composition and purity of the material being tested. Finally, depending on the peculiar properties of the drug, special studies are required.

This range of studies is needed to establish that a drug does no harm which can't be anticipated before it's licensed and put on the market. Such standards guard against surprises. Just because a drug creates no

short-term acute illness, for instance, doesn't mean it won't have an impact over time; latency periods of as long as 18 months have been reported in the scientific literature.[78] Unfortunately, the data package submitted on behalf of rbGH fails to meet the comprehensive scientific standards designed to protect health.[79]

It is unlikely that scientific shortcomings in data packages can ever be overcome in the case of rbGH. Even if the company scientists had done their best to produce a comprehensive data package, the relevance of that data package for evaluation of rbGH's human safety impacts would remain limited. That's because drug applications on farms rarely conform to test conditions.

Both common sense and the law require that data packages be based on laboratory studies or studies in confined fields under controlled conditions. The drug has not yet been licensed for use by members of the general public in the general environment, so the studies must respect this limitation on evidence which scientists can gather. It is to be hoped that laboratory studies and studies in confined fields will predict what might happen in the real world once a drug is licensed. But there is no guarantee that lab tests will be replicated in real-life experiences.

The circumstances for which rbGH might have been licensed were far from the test environment in at least two respects. First, rbGH is not a therapeutic drug, but a production drug, used solely to boost milk production, not heal a cow's illness. Therefore, it would have been administered by farmers, not veterinarians trained in procedures of drug prescription, administration and monitoring. Each farmer would have been free to use as much, or as little, of the drug on as many, or as few, of his or her cows as desired. Secondly, the milk produced from injections of rbGH was to be unlabeled and pooled with normal milk from normal cows. This would have made it all-but-impossible to conduct follow-up epidemiological studies.

When a drug is to be released into such an unregulated environment, where the standard parameters for careful assessment are beyond control, only the highest standards for data packages can offer any hope that public health will be protected. Instead, Health Canada accepted a data package that failed to meet modest standards. If this is allowed to create precedent, an entire tradition of toxicology assessment is at risk.

[78] C.E. Rogler, D. Yang, L. Rossetti, J. Donohoe, E.Alt, C.J. Chang, R. Rosenfeld, K. Neely, R.Hintz,, Altered body composition and increased frequency of diverse malignancies in insulin-like growth factor II transgenic mice, Journal of Biological Chemistry, vol. 269 (19), May 13, 1994

[79] Rbst (Nutrilac) GAPs Analysis Report, by rbST Internal Review Team, Health Protection Branch, Health Canada, page 28, April 21, 1998

Section 5:

"It is strange that in the philosophy of science there seems to be very little discussion of the evaluation of taxonomy. But we are constantly putting things which are alike into different taxonomic boxes and putting things which are different into a single taxonomic box." K. Boulding, Towards A New Economics: Critical Essays on Ecology, Distribution and other Themes.

Re-assessment One: Comparing Synthetic RbGH to Natural BGH

Regulatory scientists need a standard point of reference to compare hormones.

Growth hormones belong to the protein family of somatolactogenic hormones.[80] There are four natural variants produced by genus Bos[81], which have either 190 or 191 amino-acids (phenylalanine or alanine-phenylalanine at the N-terminal) with a heterogenicity at position 127 of the chain (valine or lucine).[82]

Soviet trials during the 1930s showed that the injection of dairy cows with pituitary-derived bovine Growth Hormone increased milk yields. However, the difficulties of producing pure pbGH made commercial application impossible. Commercialization only became viable during the 1980s, when large quantities could be produced using recombinant DNA processes.[83] Four drug manufacturers have created rbGH with varying amino acid profiles at the end of each protein except for one; terminal refers to the amino acid entity at the end of the protein chain:

[80] Report on the Public Health Aspects of the use of Bovine Somatotropin, Scientific Committee on Veterinary measures Relating to Public Health, page 4, March 15-16, 1999

[81] P.J. Eppard, L.A. Bentle, B.N. Violand, S.Ganguli, R.L. Hintz, L. Kung Jr., G.G. Kriyi, G.M. Lanza, Comparison of the galactopoietic response to pituitary-derived and recombinant derived variants of bovine growth hormone. Journal of Endocrinology, vol. 132, pages 47-56, 1992, see also Jusekvich and Guyer, 1990, also W.C. Leibhardt, The Dairy debate, page 69-70, 1993

[82] See footnote 82

[83] J C. Jusckevich, C.G.Guyer, Bovine Growth Hormone: Human Food Safety Evaluation, Science, Vol. 249, pages 875-884, 1990

Table 6	
Company	**Number of Differences in Protein**
Monsanto	1 amino acid (terminal)
Elanco Eli-Lilly	9 amino acids (terminal)
Cyanamid	3 amino acids (terminal)
UpJohn	none

Note: Terminal refers to the extra amino acids at the end of a peptide or protein chain.

Source for Table 5: Residues of some Veterinary Drugs in Animals and Foods. Monographs prepared by the Fortieth Meeting of the Joint FAO/WHO Expert Committee on Food additives, June 1992

Eppard[84] shows different production impacts of rbGH and pbGH on target animals. By adding or deleting amino acids, varying milk yields were proven to occur. This effect was confirmed by Bauman, et al, 1985, who deleted 1-4 amino acids within a natural variant of pbGH.[85] It is scientifically feasible to alter the amino acid profile of natural variants by adding extra amino acids to create more production or impact. It is an important toxicological note that within the scientific literature (i.e., Moore, et al 1988) there are warnings about tampering with the profiles of proteins or poly-peptides. For example, vasopressin analogs differing by only one or two amino acids have different antidiuretic and pressor activities; likewise, the addition of an arginine residue to the N-terminus of the A-chain of insulin results in decreased biological activity. As well, under certain conditions, the amino-terminal residue of a poly-peptide influences its *in vivo* half life.[86] Another example of rbGH alteration was done by Violand,[87] et al 1994, where it is shown that amino acid #144, normally lysine N, creates a new characteristic called epsilon-N-acetyllysine.

These deliberate alterations call into question exactly what is being analysed. For example, the JECFA fortieth meeting describes the amino acid sequence of bGH as one profile, not a compilation of profiles. These studies are included in Health Canada's assessment of rbGH, even though they are not relevant.

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[84] P.J. Eppard, L.A. Bentle, B.N. Violand, S.Ganguli, R.L. Hintz, L. Kung Jr., G.G. Kriyi, G.M. Lanza, Comparison of the galactopoietic response to pituitary-dervied and recombinant derived variants of bovine growth hormone. Journal of Endocrinology, vol. 132, pages 47-56, 1992, article received in 1991

[85] D.E. Bauman, P.J. Eppard, M.J. DeGeeter, G.M. Lanza, Responses of high-producing dairy cows to long term treatment with pituitary somatotropin and recombinant bovine growth hormone, Journal of Dairy Science, vol. 68, 1352-1362

[86] J.A. Moore, C.G. Rudman, N.J. Maclachlan, G.B. Fuller, J.W. Frayne, Equivalent potency and pharmacokinetics of recombinant human growth hormones with or without and n-terminal methionine, Journal of Endocrinology, Vol. 122, No.6 pages 2920-2926

[87] B.N. Violand, M.R. Schlittler , C.Q. Lawson, J.F. Kane, N.R. Siegel, C.E. Smith, E.W. Kolodziej , K.L. Duffin, Isolation of Escherichia coli synthesized recombinant eukaryotic proteins that contain epsilon-n-acetyllisine, Protein Science, Vol.3, No.7, pages 1089-1097, July, 1994

This indicates a common problem with rbGH research, which results from the absence of a stable point of evaluation. There are similar problems with reports of dosage rates and injection times; they are all over the map, when all that was required for safety assessment purposes were studies using the proposed 500mg. injection every 14 days of the specified drug profile.

Section 6, Part A:

"People seem to implicitly assume that the information that is most easily available to them is also the most relevant information. They often fail even to think through the possible implications of information that would be harder to get. Psychologists call this the availability bias." J.E. Russo, P.H. Schoemaker, Decision Traps: The Ten Barriers To Brilliant Decision-Making And How To Overcome Them, 1989

Re-assessment Two: Insulin-like Growth Factor-1 in Milk from rbGH Modified Cows

IGF-1 levels in modified cows are not within the normal ranges of a lactating genus Bos. The higher levels of IGF-1 are not digested within a human's upper intestinal tract. High levels of IGF-1 are associated with increased cancer risks. This calls into question Health Canada's judgement that rbGH poses no human health risks.

Most people are surprised when they find out that Health Canada rejected the application to licence rbGH strictly on the grounds of the drug's possible harm to animal health. Canada's regulators did not undertake serious research on the human health implications of rbGH use. Instead, they relied on the judgement of the Joint Expert Committee on Food Additives, an international body with no jurisdiction in Canada, which holds that rbGH creates no known risks for human health. As it turns out, JECFA's findings are flawed in several fundamental respects.

The risk from high levels of Insulin-like Growth Factor-1 in rbGH milk is the most hotly contested issue in the rbGH debate. The debate is of grave concern for public health agencies in Ontario[88] and elsewhere because high levels of IGF-1 are linked to cancer.

Despite the intensity of debate, there is a scientific consensus around the following six factors about IGF-1:

1. It is a normal constituent in the milk of all mammalian species;

2. It is within mammalian saliva and blood;

3. It has a wide range of actions within the body. For example, it regulates transport processes (ion fluxes, glucose and amino acid uptake by cells, macromolecular synthesis of RNA, DNA, proteins and lipids), as well as cell division and differentiation;

[88] Motions at the Annual General Meetings of the Association of Local Public Health Agencies of Ontario, 1994 and 1995,

4. It is required for the establishment and maintenance of tumours;

5. Bovine IGF-1 and Human IGF-1 are structurally identical proteins of 70 amino acids;[89]

6. Scientific understanding of IGF-1 is still developing within the scientific community.[90] IGF is a highly complex protein with facets yet unknown; therefore, the general trend is to proceed with caution. Even professionally-controlled therapeutic uses are dubious.

Despite this consensus, regulators have often argued that there are no human safety issues linked to the higher level of IGF-1 in the milk of genetically modified cows. They claim:

1. That IGF-1 is within normal ranges of a cow's lactation;

2. That IGF-1 levels are greater in human breast milk;

3. That IGF-1 will be digested in the human stomach.

But IGF-1 levels of rbGH modified dairy cows are not within normal ranges of bred cattle. The data shows that IGF-1 levels always increase in injected animals. The Scientific Committee on Veterinary Measure Relating to Public Health of the European Commission makes this clear in its review of 60 pieces of literature relating to IGF-1 in milk.[91]

Dairy cattle, due to genetic differences, have variable levels of IGF-1 in their milk. As well, levels of IGF-1 vary over time. To simplify, there are three main parts of a lactation: pre-parturition, parturition (birth, which involves colostrum milk), and the normal lactation. This lactation period is standardized between 305 days and 365 days. A dairy cow calves, starts milking, gets re-bred to have another calf at around day 45-90 of her lactation, and is dried off or ceases to milk for a rest period of approximately 60 days. Colostrum milk begins approximately two weeks before calving and ends 3-5 days after calving. Typically, IGF-1 pre-partuition levels are as high as 300ng/ml in milk, drop to 25ng/ml of milk at the end of the first week of calving, then drop to 1-5 ng.ml. at day 200 of a lactation. The literature is conclusive on this point.

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[89] A. Honegger, R.E. Humbel, Insulin-like growth factors I and II in fetal and adult bovine serum, Journal of Biochemistry, Vol. 262 (2), pages 569-575, 1986, See also J. Zapf, E.R. Froesch, Insulin-like growth factors/somatomedins: structure, secretion, biological actions, and physiological role. Hormone Research, Vol. 24, pages 121-130, 1986

[90] For an excellent summary of considerations showing the complexity of IGF-1, IGF-II and the influence of the binding proteins go to http:// europa.eu.int/comm/dg24/health/sc/scv/out19_en.html.

[91] Report on Public Health Aspects of the Use of Bovine Somatotropin, Consumer Policy and Consumer Health Protection, Scientific Committee on Veterinary Measures relating to Public Health, The European Commission, March 15-16 1999, go to http://europa.eu.int/commdg24/health/sc/scv/out19_en.html

pre-parturition colostrum milk 2 wks. prior to calving	parturition or birth colostrum milk from calving day - 2 wks.	normal milk 2 wks. to 305 days	avg. Bulk tank reading before rbGH use in the U.S.
100- 300 ng/ml	17 - 34 ng/ml	1- 5 ng/ml	4.3 ng/ml

The literature is also in agreement on elevated levels of IGF-1 in dairy cattle injected with the drug, as noted earlier. Despite this, many regulators still maintain that IGF-1 is within normal ranges. This is not possible. The literature shows IGF-1 increases of 75%, 200%, 360% and even 700% within an injection period.

In order to ascertain that IGF-1 levels are within normal ranges, farmers would need to establish each dairy cow's IGF-1 level first, and inject only cows that are at the top of the range of IGF-1 levels in bred cattle. That way, low IGF-1 producing cows would be forced to stay within the maximum range. However, technology to determine IGF-1 levels of each cow for practical use on the farm does not exist. Whether farmers using rbGH know their cows' individual levels is not critical. What is critical is the net result that IGF-1 will always be elevated beyond normal ranges, as illustrated below.

An imaginary case study of two cows illustrates the point. The two cows are Betsy, a high milk producer and Belle, a low milk producer. Betsy has an inherent IGF-1 level of 5 ng/ml of milk during the potential injection period time (day 120 to day 265). Belle has as a natural level of 1.5 ng/ml of milk during the potential injection period time. If Belle were injected with rbGH, then the average two-fold increase (as expressed by Burton, et al 1994[92]) would elevate her IGF-1 level to 4.5 ng/ml of milk. Comparing modified Belle to Betsy, we would see what proponents of the drug claim: that 4.5 ng/ml of IGF-1 is within the established range (1-5ng/ml) in unmodified cows such as Betsy. The problem is the lack of control to stop a farmer from injecting Betsy as well, and elevating her IGF-1 levels from 5 ng/ml to 15 ng/ml of milk.

What has been overlooked, as expressed continually in this report, is that no-one can control the farmers, because farmers do not have the technology to evaluate their own cattle. They become a variable factor themselves, negating any claim about normal ranges.

In countries allowing the use of rbGH, measurable standards of known normal ranges have been effectively eliminated. A dual range of IGF-1 levels between bred cattle and modified cattle has been created. This means there is an increase in the mass yield of IGF-1, which increases exposure of unbound and biologically active IGF-1 well beyond what's normal to milk consumers.

As defence against this argument, proponents of the drug, and some regulators, claim that human breast milk contains higher levels of IGF-1 than rbGH modified cow milk. While true, this is irrelevant, because there is no comparison in exposure time. Milk is consumed for a lifetime in many cases, while nursing commonly lasts less than a year. And IGF-1 does play a role in neonatal gut development, a role that is not normally needed beyond infancy.

[92]Burton, J.L. McBride, B.W., Block, E., Glimm, D.R., Kennelly, J.J., a review of bovine growth hormone, Journal of Dairy Science, vol. 71, 167-201.1994

Comparison of human consumption -breast milk vs. bovine milk		
Breast milk day 1 to 365	Bovine milk 3 months to adult	net difference in exposure time 25 -70 years

Originally, proponents of rbGH and regulators who claimed IGF-1 would be digested failed to recognize that milk contains casein, which will bind onto IGF-1. On its own, IGF-1, a protein, would be digested, as in meat tissue. But recent literature (Xian, et al 1995[93] and Kimura, et al 1997[94]) shows how casein can protect IGF-1 from being digested in the upper gastro-intestinal tract. Kimura also shows that recombinant human IGF-1 (remembering that human and bovine IGF-1 are identical) may be absorbed by absorptive-mediated endocytosis, rather than receptor-mediated endocytosis. As a result, a considerable amount of recombinant human IGF-1 (rhIGF-1) is absorbed into the systemic circulation. The bio-availability was 9.3%. The administration of a casein increased that figure by 67%.

The importance of IGF-1 levels in relationship to cancer risk, specifically prostate cancer, is shown by Chan, et al 1998[95], who establish that IGF-1 is a mitogen for prostate epithelial cells; associations between plasma IGF-1 levels and prostate cancer risk were also investigated. The findings were that men within the top 25% of the study group (152 controls and 152 cases) had a higher relative risk than men in the lowest 25%. From this study, the authors conclude that plasma IGF-1 levels serve as a predictor of prostate cancer risk.

Because casein protects IGF-1 from digestion, allowing free and unbound IGF-1 to be absorbed into the circulatory system, and because a sizable number of people consume milk products every day, exposure to daily elevated levels of IGF-1 beyond normal consumption rates can be expected to increase cancer risks.

The latest JECFA meeting (see Appendix C) dismissed the need for a full review of IGF-1 in dairy cows' milk. The premise for this conclusion failed to recognize that levels JECFA used to establish human safety were based on massive exposure rates to IGF-1. This assumption lacks support within the scientific literature. Within IGF-1 literature, it is now established that IGF-1 can be more potent at low levels, than high levels. As an example, Blum, et al 1989,[96] established that IGF-1 and II are bound to specific carrier proteins in the

[93] C. J Xian, C.A. Shoubridge, L.C. Read, Degradation of insulin-like growth factor-1 in the adult rat gastrointestinal tract is limited by a specific antiserum or the dietary protein casein., Journal of Endocrinology, vol. 146, pages 215-224, 1995

[94] T. Kimura, Y. Murakawa, M. Ohno, S. Ohtani, K. Higaki, Gastrointestinal absorption of recombinant human insulin-like growth factor-1 in rats., Journal of Pharmacology and Experimental Therapeutics, vol. 283, No. 3, pages 611-618, 1997

[95] J. M. Chan, M.J. Stampfer, E. Giovannucci, P.H. Gann, J. Ma, P. Wilkinson, C. H. Hennekens, M. Pollack, Plasma insulin-like growth factor-1 and prostate cancer risk: a prospective study, Science, Vol 279, No. 5350, Issue 23, pages, 563-566, Jan. 1998

[96] W.F. Blum, E.W. Jenne, F.Reppin, K. Keitzmann, M.B. Ranke, J.R. Bierich, Insulin-like growth factor-1 (IGF-1)- binding protein Complex is a better mitogen than free IGF-1, Journal of Endocrinology, Vol. 125 pages 766-772, 1989

circulatory system. The conclusion was that somatomedin binding proteins (SmBP) act as reservoirs, which release continuous low amounts of IGF-1 and appear to be a better mitogenic stimulus than temporary large concentrations of IGF-1.

It is crucial to use actual exposure rates for the population in milk from rbGH modified cows. The JECFA figures of human consumption rates of 1.5 litres a day of milk, creating a half life period of 0.5 to 2.5 hours, are not appropriate, because people consuming that amount of milk do so over extended periods (breakfast, lunch, breaks and dinner); therefore the exposure rate of .5 to 2.5 hours should be multiplied by a factor of at least three.

Remarkably, regulatory agencies, together with proponents of rbGH, have failed to demonstrate population models to determine safety. It is clear that milk has a major role in the human diet, but no agency has shown consideration for these levels of IGF-1 in relation to human populations.

TFPC has identified three main exposure groups:

1. The farm family using rbGH on their dairy cows. Under Canadian law, the farm family can consume unpasteurized milk or milk products. Therefore, the primary exposure group to rbGH modified cows milk would be dairy farm families incorporating this drug and drinking milk from their own bulk milk tank.

2. Consumers purchasing milk from a processing plant receiving milk from an area of high rbGH usage.

3. The general public purchasing milk from a processing plant receiving milk from an area of low rbGH usage.

The above are ranked in order of exposure to the drug's effects. There are also vulnerable populations within each main group:

1. People with cancer, or at risk of cancer
2. Pregnant women and the foetus
3. People suffering from acromegaly
4. Diabetics

The absence of such investigations is unacceptable given the importance of considerations around IGF-1 in the rbGH debate.

Section 6, Part B:

"The approach taken by regulatory scientists can be contrasted with that of scientists engaged in basic research, who are more likely to question the assumptions from conventional science and to require empirical support for them ... rather than to make comparisons with the existing context in order to generalize from limited experimental data." L.N. Mills, "Science and Social Context: The Regulator of Recombinant Growth Hormone (rbGH) in the United States and Canada, 1982-1998," University of Toronto, PhD Thesis, 1999.

Estimates of Bio-available IGF in Human Serum and Lymph Associated with Ingestion of Milk From rbGH Cows: A Re-consideration of JECFA'S* Interpretations,**

By: Eve Shulman, M.Sc, Ph.D, D.E.C.H.

Health Canada accepted the judgement that rbGH posed no threat to human health, even though levels of Insulin-Like Growth Factor-1 are high in rbGH milk. There are now many grounds on which this judgement can be challenged.

As described earlier in Section 6 (and elaborated in the Appendix), IGF, its binding proteins (BPs) in blood and tissues, its receptors on target cells, and its extended growth-factor family form a complex physiological and regulatory system. Though IGF alone is not vital to life, this system is essential for trophic growth, development and differentiation of tissues and organs, as well as the regulation of cell division and functions. However, as with most things in life, there can be too much of a good thing, as well as too little. Physiological or clinical (pathological) excesses and deficiencies in IGF are associated with higher risks of select cancers and pathological states.

The vascular system is the main carrier (transport) and storage place for native (endogenous) IGF, which is produced in the tissues. The vascular pool of IGF is approximately 1.225 million ng in adult males; the tissues produce close to one million nanograms IGF daily, to replenish the plasma pool and maintain its concentration.

The main source of external (exogenous) IGF is ingestion of food that contains IGF, such as milk and meat which have not been processed through prolonged high temperatures or high acidity.

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* Joint Expert Committee on Food Additives (FAO/WHO)

** Bibliography for Section 6, part B, is produced in Appendix A.

The amount of IGF in milk varies with many factors; normal concentrations range from 3-4 to10-15 ng/ml. Much of the ingested IGF is absorbed by gut tissues (which have IGF receptors, high affinity, and are highly responsive to IGF), and when a proportion of the exogenous IGF passes via the portal system to the liver and the arterial circulation.

It has been confirmed that at least 10% of the ingested IGF reaches the peripheral circulation system intact. For milk from rbGH cows, with a concentration of 13 ng/ml IGF; [97] of exogenous IGF delivered to the serum, the daily dose is1,950 ng, or close to 0.1% total serum IGF pool.

There are subtle binding differences, but otherwise little distinction in structure, activity or disposition of endogenous and exogenous IGF respectively.

In 1998-99, JECFA ruled that rbGH milk was safe for human consumption, insofar as there was no direct evidence to the contrary. This decision can be successfully challenged scientifically, on the following grounds: (a) lack of evidence on long-term effects of prolonged ingestion of excess IGF[98] (for example, in rbGH milk); (b) clinical and pathological observations, particularly the recent genetic findings that chronically elevated serum IGF (regardless of its source) is a risk factor for the eventual development of colon and breast cancer in humans; (c) accumulating knowledge on the regulatory mechanisms of the IGF system in the blood, and on the auto-regulating capacity of IGF to increase its bio-availability; (d) demonstrated IGF allergenic and immunological activity; and (e) the observation that ingested IGF is absorbed, and does reach the peripheral blood stream as well as the interstitium extravascular spaces, in intact form. Additional grounds include higher antibiotic levels in rbGH milk, and the rise in antibiotic-resistant strains of bacteria.

JECFA also claimed that the excess concentration of IGF in rbGH milk is a negligible proportion of serum endogenous total IGF. The Committee did not distinguish between bio-available and non-bio-available forms of serum IGF.

In this follow-up to the JECFA analysis, the two categories of serum IGF are taken into account. The purpose is to estimate the proportion of bio-active IGF in serum that is attributable to ingested milk-borne IGF. Only the effects of excess/exogenous IGF on IGF bio-availability are considered, rather than effects on all tissues, organs and physiological systems.

JECFA estimates were derived on the basis of one daily dose (rather than the more realistic multiple doses of real-life milk consumption) of excess IGF ingestion on IGF bio-availability in serum or tissues. This limits predictions regarding long-term bio-activity and disposition of milk-born excess IGF in serum and tissue. Nevertheless, it is valid starting point.

[97] As determined by JECFA.

[98] Beneficial development effects of colostrum (containing high IGF levels) have been demonstrated in newborns only.

Given the single-dose in this review design, along with the recent information on mechanisms of IGF bio-availability, it can be reliably predicted that the estimates shown in the tables below are minimal estimates, and that both the milk-borne IGF, and its bio-availability in serum will be increased during periods of prolonged rbGH milk consumption.

The estimates were developed from two distinct lines of evidence:

1. The first line of evidence deals with the disposition of intravenous (iv) or subcutaneous (sc) injection of single or multiple doses of IGF, in normal or sick individuals. These studies were conduced in Switzerland, France, the USA, Australia and Japan during the late 1980s and throughout the 1990s.

   These researchers measured the levels and disposition of the injected IGF in the blood, and the effects on native (endogenous) serum IGF. Some reported on the level and regulation of the IGF binding proteins (IGFBPs); others noted the crossing of injected IGF through the capillaries, into tissues or lymph (interstitium), as well as hormonal or metabolic effects of the exogenous IGF.

2. The second line of evidence comprises animal experiments, and is dedicated to the oral feeding or orogastric research. A diversity of test animals (mouse, rat, calf, cow, sheep, piglet and monkey), IGF detection tests/assays, and experimental design were used.

In both lines, only results from *in vivo* studies were included. Furthermore, there was no attempt to integrate the three different modes of administration (iv, sc, and oral). Rather, the time-curves of the exogenous serum IGF, administered either by iv bolus or feeding, are shown as distinct, alternate estimates.

Surprisingly, despite the many sources of differences among researchers and across studies, several clear trends and patterns were indicated. These form the scientific framework for estimations here. (See Technical Note.) For the sake of caution in projecting from multiple sources and across animal species, the lower confirmed values reported in the studies were applied here.

Ultimately, the cumulative effect of systematically applying lower rates and proportions are expected to seriously underestimate the exogenous milk-borne IGF bio-availability, even for a single (daily) dose.

This approach, along with the design of the analysis, raises the following issues in interpretation of the estimates:

A. <u>Absorption Rate of Ingested Milk-Borne IGF</u>

   The absorption rate of 10% used here lies in the 4-12% range reported in the literature. The figures are arguably too low. The addition of casein as a milk supplement, in the same concentration occurring naturally in cow's milk, can boost absorption as much as seven-fold.

The mechanisms underlying milk IGF absorption have been described, and they support absorption rates greater than 10%, insofar as these are largely determined by enzymatic and proteolytic inhibitors in the milk, on the one hand, and the concentration of exogenous free IGF in the gut, on the other hand.

Moreover, IGF concentration in rbGH milk is higher than the 13ng/ml value used by JECFA and in the current estimates.

A small increase in the absorption rate (to above 10%) can make a sizeable difference in the estimated bio-availability of rbGH milk-borne IGF.

B. Distribution of IGF Binding Proteins (IGFBPs)

The BP distribution of the exogenous IGF used in the iv-based estimates (60% large complex; 30% serum small complexes; 10% serum free IGF) yields the highest baseline for serum bio-available endogenous IGF[99]. That means that the proportion of exogenous bio-available IGF will automatically be depressed.

The most common serum endogenous IGFBP distribution reported in humans is 90% large complex; 9%-10% serum small complexes; <1% free IGF. Had this distribution been applied[100], the low baseline for endogenous bio-available IGF (approximately 10% of serum total IGF) would increase the estimated proportion of exogenous bio-available IGF from milk two-to-four fold, raising it to well above 1%.

C. Predictors of bGH Milk-Borne IGF Bio-Availability in the Long-Term: Multiple Doses

Most of the oral feeding studies, the human IGF injection studies, and the current estimates are based on a single (or daily) dose of exogenous IGF. With one or two exceptions, the multiple-dose studies involved five-to-ten days exposure.[101] This is not the same order of exposure to exogenous IGF as that of daily consumption of rbGH milk-borne IGF, over a lifetime.

Nevertheless, the unexpected recent finding, even with short-term multiple doses -- namely, the tendency of exogenous IGF to actively regulate and increase its bio-availability in and outside the serum, the sensitization to cumulative dosing with IGF, and the longer-than-predicted survival of bio-active IGF in serum and gut -- all support the expectation that regular consumption of rbGH milk-

[99] Compared with other reported distributions.

[100] This distribution (90%-9%-1%) could not be used as a model for computing estimates here, as the source studies did not show time-concentration curves for IGF.

[101] These studies were not included in the estimates due to the lack of time-concentration curves or B.P. distribution.

borne IGF will result in far greater bio-available IGF in serum and tissues over time than the close to 1% contribution estimated here.

In summary, how should the estimates be interpreted?

Reports on proportions of exogenous serum IGF bio-availability in the literature range from 0.03%-3%. The estimates shown in Tables 1.1 and 2.1 range from 0.27% - 0.67% (based on human i.v. time-concentration curves) and from 0.33% - 0.82% (based on animal oral feeding rates).

These values, close to 1%,[102] may be partly influenced by species differences, but more likely by dose, the serum endogenous BP/IGF distribution model, and the single dose design.

Notwithstanding the fact that the estimates are minimal and single-dose, exposure to 1% excess bio-active IGF in serum is not negligible, in view of the demonstrated ability of cells and tissues to react to nanomolar and even picogram concentrations of exogenous IGF.[103]

Secondly, even the limited, short-term multiple dose studies indicate a hitherto unexpected IGF bio-availability "machine," which actively increases bio-availability of exogenous IGF (as well as aspects of endogenous IGF) to tissues; such activity and the survival of bio-active IGF is more prolonged *in vivo*. Thus, estimates for a single dose have to be multiplied, although we do not yet know the factor of increase, nor the shape of its time-curve. This is a critical consideration[104].

In view of the above, the proportion in serum of bio-active IGF from rbGH milk ingestion must be interpreted physiologically and clinically, as well as statistically, to meet the criteria of sound science and responsible decision-making[105] regarding the safety of prolonged exposure to excess, exogenous IGF in humans.

[102] This is almost 10-fold greater than the JECFA estimate, in which the time-frame of ingestion was not given.

[103] Moreover, this reactivity does not become refractory, as there is no oversaturation when cells are exposed to "tiny" doses, over a prolonged period.

[104] The consideration is based more on mechanical and empirical mio-port, evidence, and less on assumption. In that sense, it supercedes the precautionary principle, which is less stringent scientifically.

[105] This applies to all national and international jurisdictions, and to their advisory, expert and consensus support groups.

Table 1-1

Estimates of Bio-available IGF in Human[a] Serum and Lymph Associated with Consumption of Milk from rBST-Treated Cows[b]

Time[c]	Exogenous Dose:	Ingestion of 1.5 L. rbST milk per day 13ng/ml IGF x 10% absorption = 1,950 ng IGF daily*								
	IGF in Serum Pool Small Complexes				Pool Serum Free IGF			A[d]	B	C
min.	%	ng	Shift to BP[e] large complex ng	Cross to lymph ng	%	ng	Cross to lymph[e] ng	Sum IGF in small complexes and free IGF ng	Sum IGF cross to lymph[f] ng	= A + B ng
0-5	60	1,170	0	0	7.6	148	0	1,318	0	1,318
120	16.8	180	363	370	0	0	74	728	444	1,172

Legend: a) Adult Humans
b) Based on Data from Intravenous (i.v.) Bolus experiments in humans. Details on computations are given in the Appendix.
c) At start, for i.v. Bolus source data and/or at steady state for estimates based on i.v. or oral experiments (Tables 2-1 and 2-2).
d) Includes shift of small complex IGF to large complex, and 50% of estimated degradation.
e) Binding Proteins.
f) Crossing capillary barrier from blood to lymph (interstitium)

* Based on JECFA Report (1999)

Table 1-2

Estimates of Exogenous IGF as Percentage of Total Bio-available IGF in Serum and Lymph[a]

	IGF: AT START (t = 0-5 min.)			IGF: AT STEADY STATE (t = 120 or 240 min.)		
	A **Serum Small Complex ng + Free IGF** **ng**	**B** **Lymph** **ng**	**C** **= A + B** **ng**	**A** **Serum Small Complexes ng + Free IGF** **ng**	**B** **Lymph** **ng**	**C** **= A + B** **ng**
Exogenous IGF from (Milk)	1.318	0	(1,318)	728	444	1,172
Total IGF in Serum or Lymph: Bio-availability[b] Model I	491,318	245,000	736,318	490,728	245,444	736,172
% Exog. Of total of IGF	0.27	-	(0.18)	0.15	0.18	0.16
Total IGF in Serum of Lymph Bio-availability:[b]	197,318	245,000	442,318	198,728	245,444	442,172
Model II[c] % Exog. Of total 1GF	0.67	-	(0.30)	0.37	0.18	0.27

Legend: a)

b) Total bio-available IGF in serum or lymph includes Endogenous and Exogenous small serum complexes IGF plus serum-free IGF.

c) For details on BP distribution Models I and II, see Table A-1 in the Appendix.

Table 2-1

Alternate Estimates of Bio-available IGF in Human Serum and Lymph Associated with Consumption of Milk from rbST-Treated Cows[a]

Exogenous Dose: Ingestion of 1.5 L. of rbST milk per day(13ng-ml IGF.) x 10% absorption = 1,950 ng IGF daily.

Time	Pool IGF in Serum Small Complexes				Pool Serum Free IGF			A	B	C
min.	%	ng	Shift to BP large complex ng	Cross to lymph ng	%	ng	Cross to lymph ng	Sum IGF in small complexes and free IGF ng	Sum IGF cross to lymph ng	= A + B ng
240	83.5	1,628	64.5	N/A[b]	N/A[c]	N/A	N/A	1,628	N/A	(1,628)
Standardized Values[d] 240	83.5	1,628	64.5	326	N/A	N/A	N/A	1,628	326	1,954

Legend: a) Based on oral feeding experiments in animals.
b) These values cannot be computed from reported data. See d below.
c) Free IGF values have been reported as "0" or negligible.
d) The "Cross-to-Lymph" values have been projected based on the observed rate of 20% in humans. These values are called "Standardized."
N/A = Not Available

Table 2-2

Estimates of Exogenous IGF as Percentage of Total Bio-available IGF in Serum and Lymph[a]

At Steady State (Standardized)[b]

	A Serum small complexes + free IGF ng	B Lymph ng	C = A + B ng
Exogenous IGF (from Milk)	1,628	326	1,954
Total IGF in Serum Lymph: Bio-Availability Model I	491,628	245,326	736,954
% Exog. Of Total IGF	0.33	0.13	0.27
Total IGF in Serum or Lymph:			
Bio-Availability Model II	197,628	245,326	442,954
% Exog. Of Total IGF	0.82	0.13	0.44

Legend: a) Based on oral feeding experiments in animals.
b) The "Cross-to-Lymph" values have been projected based on the observed rate of 20% in humans. These values are called "Standardized."

Section 7:

"... Always be cautious about information you read in magazines or newspapers printed outside of Canada, as well as radio and TV broadcasts originating from non-Canadian stations." The Eating Edge: A Guide To Healthy Eating For Teens, grades 9-10 Ontario curriculum guide, sponsored by the Ontario Milk Marketing Board.

"Overstocking"- A violation of animal health

RbGH not only violates basic principles of animal health. These violations run counter to established Canadian dairy regulations and laws.

Health Canada rejected the application to license rbGH because of concerns about animal health.

There is little need to add new information, because there is little controversy around the matter.[106] The drug companies concede the point, and list cautions or warnings to this effect on their labels. The U.S. FDA likewise acknowledges the ill-health effects associated with the drug's use, though it is claimed that these effects can be "managed."

What's most significant and worrisome from the perspective of this study is Health Canada's failure to assess ill effects on animal health in light of basic laws and principles of Canadian dairying. In dissenting from the U.S. FDA decision and asserting a distinctively Canadian viewpoint, Health Canada failed to acknowledge the heritage that gave rise to that distinctive Canadian viewpoint. That heritage allows an assessment of the links between animal and human well-being.

[106] Cf. D.S. Kronfeld, Health management of dairy herds treated with bovine somatotropin, Journal of the American Veterinary Association, Vol. 204, pages 116-130, 1994; P. Willberg, An international perspective on bovine somatotropin and clinical mastitis, Journal of the American Veterinary Association, Vol. 205, No.4, pages 538-541, Aug. 15, 1994; Ontario Dairy Regulations 761, section 52, (3)Consolidation of Regulations under the Milk Act, Nov. 1997

It's well-recognized, for instance, that rbGH injections lead to the dairy animal's increased ingestion of feed.[107] This, in turn, is commonly linked to stomach disorders which is recognized side effect of rbGH use. Stomach disorders, according to classic texts on butter quality, can cause milk to become thin, bluish and bitter.[108] This being the case, rbGH should have been automatically disqualified because of its violation of Canadian standards around milk quality.

Likewise, the use of rbGH is almost universally associated with increased rates of mastitis among cows. Mastitis, an infection of the cow's udder, requires treatment with antibiotics. Increased use of antibiotics jeopardizes their potency and effectiveness, an ominous trend that encourages "superbugs" which threaten human health. Increased mastitis rates also run counter to the Ontario Milk Act, which discourages increased somatic cells.[109]

Mastitis needs to be recognized as a manifestation of larger problems in a dairy operation, not, as is assumed by the U.S. FDA, a "side effect" that can be "managed" with other drugs. The widespread incidence of mastitis among cows injected with rbGH should be alerted Health Canada officials to other likely violations of Canadian dairying law and practice. Overloading of the cow's udder (overstocking, as it was once commonly called), for instance, is frequently linked to mastitis. The overstocking that's standard among cows injected with rbGH, regardless of other farm management practices, indicates that milk yield does not derive from normal cows, whose production has been increased by breeding. In the case of cows injected with rbGH, milk yields are a function of the drug, not the cow herself. When all is said and done, that's what rbGH is about: cows are not in control of their own metabolism, and their milk does not come from their normal or inherited capacities. This, again, is a clear violation of longstanding Canadian practices enforced by law.

In the United States, it's become the norm to regard the negative impact of drugs on animal health as "side effects" which can be "managed." This view is not as widely accepted in Canada, perhaps due to a legacy which held overstocking to be, as expressed in Black's Veterinary Dictionary, a "cruel practice." As far back as 1877, mastitis was attributed in Canada to improper care, overstocking, and unethical practices.[110] The same view was then standard in U.S. circles.[111]

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[107] Posilac Manual, for example.

[108] Milk, Paul G. Heinenoon, PhD, Director of the Laboratories of the United States Serum Company, 1919. Cf. Also. Ontario Ministry of Agriculture, Bulletins 479-494, especially bulletin 484, p. 7, Jan. 1952, A Guide to the Production of High Quality Milk.

[109] Ontario Dairy Regulations 761, section 52, (3) Consolidation of Regulations under The Milk Act, Nov. 1997.

[110] Professor J. Law, V.S., The Canadian Farmer's Veterinary Advisor, entered according to the Act of the Parliament of Canada, by A.H. Havey in the Office of the Minister of Agriculture, 1877, page 256.

[111] Diseases of Cattle, Special Report, United States Department of Agriculture, Bureau of Animal Husbandry, 1909.

A widely publicized case at the turn-of-the century rendered this judgement following the death of dairy cattle at a farm exhibit in Canada:

> **Some Valuable Cows Die at the Fair**
> **Cause is purely local, No Contagious Disease Existed.**
>
> In order to quell rumours that a contagious disease existed, killing several animals, a committee consisting of Andrew Smith, V.S., Hon. John Dryden and John I. Hobson presented the following report.
>
> The Cattle Committee today received the report of the veterinaries appointed to investigate the cause of mortality among cattle. The report showed the cause of death to be entirely local, no disease of a contagious character existing among any of the cattle affected. The death in each case had been caused by too much forcing and manipulation of the udder with a view to improve its appearance, coupled with extreme heat at the time. In each case it was a voluntary act by those in charge leading to a very great loss to the owners.
>
> We have no desire to make any comment on this report other than to state that we trust the present instance will be a valuable lesson to those who adopt such practices as indicated above in order to gain favour in the prize ring. It is only fair to the Industrial Exhibition Association and to the breeders of this province to give the fullest publicity to this report in order to set matters right with the exact cause of the loss of so many animals, and to show no disease of a contagious character existed.[112]

Respect and appreciation are due to those who investigated the ill effects of rbGH on animal health. Yet it remains a matter of concern that Health Canada did not assess these findings in light of Canadian laws and traditions.

[112] Farming, A Paper for Farmers and Stockmen, Vol. XVII, No. 2, Sept. 12th, 1899, page 65.

Section 8:

"To know that we know what we know, and that we do not know what we do not know, that is true knowledge." Confucius

Conclusion: Towards a Re-Affirmation of Milk Quality

To protect public health, a new definition of milk is needed, a definition that assures both security and progress.

Canada's dairy farmers support an 8 billion dollar-a-year industry, providing a range of home-grown products that come with the blessing of most nutritionists and with official approval from Canada's guidelines for a healthy diet. The industry's enviable reputation and the public's health depend on constant attention to the fundamentals and details that make for the excellence that has earned this approval.

The need for precaution and security can run counter to the desires of innovators. For instance, there is no end to the well-meaning desire to take advantage of the fact that milk products are a staple of the Canadian diet, accounting for 14 percent of all food and beverage sales. Fortifying milk with Vitamin D was long ago considered the surest way to make sure all Canadians consumed enough Vitamin D. A new generation of fortifiers believe essential fatty acids from fish should be put into milk.[113]

When the natural boundaries that once identified certain nutrients with certain foods are ruptured, there is no limit to innovation. Genetic engineering is about the systematic disruption of these natural boundaries. The end of the technical limits brought about by genetic engineering puts even more importance on legislative limits; since technology and nature no longer "legislate" limits, governments must. Precisely because of genetic engineering, Canadian regulators protecting the public's safety must turn their minds to the strengthening and renewal of regulations. Strengthening and renewing the definition of milk is as good a place to start as any.

There are many reasons why longstanding approaches to the definition of milk need to be clarified and strengthened. To begin with, there are at present too many definitions with too little co-ordination. Definitions within Ontario's Health Protection and Promotion Act don't always conform to all clauses in Ontario's Milk Act, or Canada's Food and Drug Act, or the National Dairy Code, or other provinces' milk acts, not to mention the International Dairy Federation or Codex Alimentarius. One standard definition would seem appropriate in today's world, where cross-border trade in once-perishable goods is common.

[113] Toronto Daily Star, July 11, 2000, pages 17-18

Secondly, some expressions of traditional definitions of milk are clearly too restrictive. Some are species-limited, such as those that define milk as coming from a cow, or even one now-defunct wild breed of cow, genus *Bos*; goat and sheep milk are thereby arbitrarily excluded. Ironically, such obsolete restrictions, by their very rigidity, have led to the toleration of regulatory drift, to the point that dairy animals modified by drug injections or hormones have become accepted. In this way, obsolete definitions have encouraged regulators to turn a "blind eye" when faced with hormones that clearly alter the performance of dairy animals. An updated definition provides more security, and a more stable point of reference, than regulatory drift.

The shortcomings in the various definitions and approaches to milk come out of a tradition which took such matters seriously and which valued both scientific precision and public safety, as we have taken pains to point out. Nevertheless, the definitions rested on some assumptions about matters that seemed self-evident at the time. People raised within the relatively parochial food culture of pre-1960s Canada assumed, for instance, that milk came from cows, not goats, sheep, buffalo or horses. Variations from one jurisdiction to another were not a grave matter prior to the days of super-highways, refrigerated trucks and global trade agreements. And no-one anticipated genetic engineering, the crossing of species barriers or the over-riding of inherited characteristics. That's why such loose words, by today's standards, as "normal" became conceptual cornerstones of dairy laws and regulations. Though some of the assumptions behind this heritage have been outpaced by events, the heritage itself is worthy of respect.

It behooves the regulators and law-makers of today to either follow the spirit of this heritage, while modernizing its specifics, or to break from this heritage comprehensively. This discussion paper, deeply respectful of our public health predecessors, promotes the option of modernizing their legacy. With this in mind, we propose the following amendment to Division 8, Section B.08.003(S) Milk or Whole Milk, of the Consolidated Regulations of the Food and Drugs Act:

Milk or Whole Milk

Section B.08.003(S) Milk or Whole Milk

(a) shall be the normal lacteal secretion, free of colostrum discoloration, known as raw milk, obtained from the mammary gland of the following species of the class *mammalia*,

cow, genus *Bos/Taurus* (See Appendix H);
goat, genus *Caprine*;
sheep, genus *Ovine*;
horse, genus *Equine*, and that;

(b) any act to modify or supplement said animal's inherent properties, from conception till death, for non-therapeutic purposes of milk or meat production is prohibited; and that

(c) the feeding of genetically-engineered feedstuffs or forages is prohibited; and

(d) that raw milk shall be fortified with added vitamin D in such an amount that a reasonable daily intake of the milk contains not less than 300 International Units and not more than 400 International Units of vitamin D.

There are several advantages to such a definition. It expands the range of mammals designated to produce milk, and includes all of them in one reference and section. It protects the integrity of the animals designated to produce milk for human consumption so that sustainable breeding practices can be maintained; consequently, drugs, hormones or genetic manipulation overriding classic (male x female) breeding are banned. It provides clear direction for farmers by limiting feeds to plants that have a proven record of supporting the biochemical profile of "normal" milk. It provides clear direction to drug companies by eliminating any doubt about modification principles or practices.

A clear definition, such as that provided above, will also bring an end to the regulatory drift that has jeopardized both the dairy industry and public health. Standing on the shoulders of scientists, regulators, public health advocates and dairy farmers of an earlier age, it also looks to the future. It outlines and reaffirms the cardinal requisites of a progressive dairy industry. It establishes and confirms a baseline for pro-active and disciplined scientific work. The legacy of the cardinal requisites and disciplined scientists has been squandered for too long. Health Canada's review of rbGH clearly shows the damage done by regulatory drift. It also highlights the need and opportunity to rebuild on a sound foundation.

Appendix A-1

A Guide to Technical Language (Lexicon)

1. B.P. COMPLEXES

In serum, IGF is generally bound to one of six binding proteins, to form complexes from which it can dissociate. The BPs are IGFBP-1 to IGFBP6.

The most common complexes are:

(A) The large ternary complex which binds IGFBP-3 and IGF, is known as the 150 KDa complex. This complex has few unsaturated sites for binding exogenous IGF; the bound IGF has a relatively long survival. Exogenous IGF can regulate and modify the production of IGFBP in the tissues, for transfer to the bloodstream.

(B) The serum small complexes (BP 1,2,4) range from 30-50 KDa. The most common is IGFBP-2. These IGFBPs have unsaturated sites which permit binding of exogenous IGF entering the bloodstream. The small complex BPs can cross the capillary barrier partially, and are the main BPs in lymph (interstitium); they have a short half-life and rapid turn-over.

A percentage of exogenous IGF, and a smaller percentage of native (endogenous) IGF, is unbound in serum; that is serum free IGF.

2. BP Distribution in Serum or Plasma

Researchers have reported various distributions of IGF among the large and small complexes, and unbound (free) IGF in serum, respectively. The three most commonly reported distributions are;

a) 90% - 9% - <1%;
b) 80% - 19% - 1%;
c) 60% - 30% - 10%, for the three types of binding (i.e., large, small, free).

The difference in these distributions may be largely explained by the variation, specificity and sensitivity of the tests used to detect free and bound IGF, but also by the nutritional status (fasting versus non-fasting) and age of subjects.

3. Bio-availability

Bio-available IGF is bio-active, intact or slightly modified IGF, that

a) can bind to binding proteins in serum, lymph and other tissues;
b) can bind to the appropriate IGF receptors on cell surface; or
c) can bind to antibodies.

IGF bio-activity can be measured by specific tests.

IFG is active only in tissues, and not in the bloodstream (i.e., not in the vascular system). Free IGF and small complexes IGF can leave the vascular system by passing through the capillary wall into the interstitium and tissues, where they can be active. These forms of IGF are called the bio-active IGFs or the bio-active serum small complexes IGF.

Only 5% of the serum IGF bound to the large BP complex can leave the vascular system (i.e., pass through the capillary barrier) to become active. Most of the serum IGF (60% - 90%) is bound to the large complex, and is not bio-active.

The distribution and pool size of BPs can determine the amount of exogenous IGF binding. Exogenous IGF that remains unbound either crosses the vascular system into the extra-vascular space and tissues, or is enzymatically degraded, or remains unbound and intact in the serum, for a variable period.

A critically important recent finding is that exogenous IGF (and endogenous IGF, under certain conditions) can modulate the amount and kind of BPs, and thus modify its own bio-availability.

4. Effects of Exogenous IGF

Endogenous IGF is regulated. The regulatory system ensures that IGF is produced in tissues (over 1 million ng daily) for transfer to the blood, to keep the serum IGF concentration and pool at a constant level.

The converse, (i.e., the transfer of serum IGF out of the vascular system and its delivery to the specific sites and tissues, as needed) is also biologically regulated.

In that context, exogenous IGF is excess IGF and may be considered to be unregulated, as it can pass out of the vascular system and bind (or block binding) in the tissues inappropriately.

To date, two types of effects of exogenous IGF have been documented, and confirmed, largely through the use of recombinant IGF, or radioactive tracers, as well as bio-chemical and historical methods and bio-activity tests.

The First Type includes effects of exogenous IGF on tissues and systems such as:

a) specific growth stimulation and functional modifications of the gastro-intestinal tract; or
b) beneficial, long-term development effects of colostrum on the newborn (colostrum contains very high levels of IGF); or
c) excluded therapeutic or pathogenic effects documented in the clinical literature.
d) reactive stimulation on the lymphoid tissues (histological and functional) affecting the immunological system.
e) transitory effects on glucose and insulin metabolism.

The Second Type is the effect of exogenous IGF on its own disposition in the serum, its bio-activity and regulation. This is referred to as the "IGF Machine." Exogenous IGF, particularly from multiple doses and long-term administration

a) increases its survival time in serum, as well as in extra-vascular tissues such as the gut (after ingestion);
b) alters BP binding activity
c) produces "accommodation," in bio-activity, under prolonged administration
d) produces sensitization, such as intensified antigenic response;
e) alters the kinetics and disposition of exogenous IGF in serum leading to higher and earlier peaks, and greater time-concentration values (Area-Under-the-Curve AUC).

All these changes in IGF activity specifically and actively lead to increased bio-availability of exogenous IGF. In other words, exogenous IGF potentiates its bio-availability. It facilitates and sensitizes the target tissues to IGF activity.

Time-Curves for Exogenous IGF and IGFBP in the Vascular System

Tracking of the concentration or pool of exogenous IGF, from the time it enters into the vascular system (i.e., from the start) until its disappearance (clearance), produces a time-concentration-curve for IGF.

Time-curves can be produced for exogenous total IGF, bound IGF, or free IGF, or all three combined, usually with the help of a tracer or bio-technologically modified exogenous IGF. The analysis here also produced:

a) time-curves for endogenous IGF, to serve as a baseline, and
b) time curves for endogenous plus exogenous IGF, to serve as bases for the estimation of the proportion of exogenous ICF of total serum bio-available IGF.

The time-curve can be divided into two main stages: transitional and steady. A peak or maximum plateau of serum exogenous IGF occurs somewhere along the time-curve, conditional to the mode of

administration of the IGF (IV, S.C., or oral) in the first place.

The early stage starts immediately at the entry of the exogenous IGF into the vascular system.

This is the transitional stage and consists of the following processes:

a) increasing binding of the exogenous IGF to the serum small complexes IGFBPs;
b) exit and transfer of the free exogenous IGF, and the small complexes-bound IGF out of the vascular system,
c) shift of the newly-bound exogenous IGF from the small complexes IGFBPs to the large complex (ternary);
d) binding of serum exogenous free IGF to large complex (as well as small complexes BPs); and degradation of the serum free IGF and small complexes-bound exogenous IGF.

The time-curves for the exogenous IGF in the transitional stage are marked by upward or downward trends that are characteristic of the distinct mode and duration of administration of the exogenous IGF.

Stabilization of the time-curve for S.C.(subcutaneous) or oral IGF administration is marked by a flattening upward curve or elevated plateau of exogenous and total serum IGF. Alternatively, under various study designs, the transitional phase ends in a peak of IGF.

The time-curve for in bolus administration is the inverse:

a) it starts with an early peak in serum exogenous IGF (concentration or pool);
b) then it declines as the exogenous free and small complexes BP bind rapidly, and
c) a prolonged, gradual rise and plateau occurs in the large complex-bound IGF, even as the total IGF decreases.

The second stage is the steady state (or equilibrium), which starts with the plateau. It signals the end of the binding and transfer processes; it can be of short duration or prolonged, and includes the dissociating and degration of IGF.

> Usually, most of the exogenous free IGF in the serum disappears during the earlier, transition phase. Also, the serum small complexes binding (of the exogenous IGF) and most of the shift to the large complex have already occurred at this time.

Despite the differences in mode of administration and concentrations or dosage frequency (single versus multiple doses), the steady state generally occurs between one to two hours after the start of IGF administration, but may occur at two to four hours, particularly for prolonged administration, multiple doses, or high concentrations. The subcutaneous mode is generally marked by a later steady state.

The total disappearance (or clearance) period also varies according to experimental factors. In sum, the time-curves for serum exogenous IGF indicate that:

i) exogenous free IGF can remain intact in the serum (or cross to the intestium of tissues) for a longer period than suggested by previous accounts; and there is greater sensitivity in BP binding in serum, in vivo, as demonstrated by the time-curves for recombinant IGF or IGF analogues;
ii) IGFBP binding of bio-active forms of exogenous IGF starts almost immediately after exogenous IGF enters the vascular system.
iii) IGFBP binding of exogenous free IGF starts with the small complexes first, and the distribution of IGF between serum small and large complexes is neither passive nor reversible;
iv) part or most of the disappearance of exogenous IGF is due to its binding to small or large complexes, or to its crossing out of the vascular system, rather than to early degradation in the blood; and that
v) exogenous IGF can raise the serum endogenous IGF levels; the extent and duration of the increase is affected by multiple doses.

Appendix A-2

Technical Notes
Estimates of Bio-availability of Ingested IGF from rBST Milk

This note presents the rationale for the estimates, description of methodologies used in deriving the estimates, an annotated guide to technical terms, and a set of principles that emerged from the literature review and analysis, which formed the scientific framework for the estimates.

1. Rationale for Producing New Estimates

IGF

IGFs are small peptiles [proteins] of approximately 7 KDa weight, that are produced normally in the tissues. The interstitium and in body fluid in large proportion enter the vascular system where they are transported to the target tissues [i.e., their endocrine function] and are stored.

A smaller pool of IGF remains in the stored interstitium close to where they were produced paracrine, and are active in tissues cells which produced them in the first place [autocrine function]; these IGFs do not enter the bloodstream.

IGFs are active only in the target tissues, where they bind to their specific, high and low affinity receptors on cell surface. In the tissues, IGFs are either "free" [unbound] or tend to bind to one of several specific small complex binding proteins [IGFBPs], under various physiological conditions and needs.

IGFBPs are also produced in the tissues* and found in fluids including cerebral vascular fluid, amniotic fluid, blood, lymph, milk.

To a large extent IGF in the vascular system is bound to large ternary complexes of which 5% cross the capillary barrier. The rest do not leave the blood. This constitutes the storage facility and transport mechanism for IGF in the blood.

During the time the IGFs are in the blood, they are not active, but preserve the potential to be so when they exit.

IGFs are continuously removed from the vascular system, either by transit into the tissues, by enzymatic degration or through excretion by the kidney

In contrast to the ternary large IGF-IGFBP complexes, free IGF in serum, and IGF bound to FBPs small complexes, can, and do go in and out of the vascular system. Injected or ingested [exogeneous] IGF belongs to the latter two categories.

Exogenous IGF

The rapid accumulation of new knowledge and understanding of the mechanisms and regulation of the IGF system, along with unanswered questions, foster controversies over the impact of exogenous IGF in humans.

Issues include the role of IGF system in cancer progression and therapy, the use of IGF as health supplements for infants and aged, and the safety of food-borne IGF in humans.

Several controversies over basic mechanisms relevant to ingested IGF are discussed below.

Issue: When exogenous IGF [i.e., IGF from external sources] enters the blood serum of the peripheral vascular system, either through injection or absorption from the gut, its activity and function are similar to those of endogenous IGF. Likewise, there is little difference in response of target cells and tissues between the two forms of IGF.

Nevertheless, in real-life, exogenous IGF is, by definition, excess IGF, and unregulated at the start. Recent studies have indicated that chronic endogenous excess IGF is a risk factor for the eventual development of breast and colon cancer in humans. The daily consumption of exogenous [excess] IGF in rBST milk may qualify as chronic excess and stimulation exposure. One variety of lymphosarcoma is directly associated with chronic stimulation by (exogenous) IGF that passes into the lymphatic system.

Issue: After the administration of exogenous IGF, once the past-steady state is reached, exogenous IGF (with exceptions) does not cause the increase in the serum baseline of endogenous IGF. The exceptions are prolonged [chronic] IGF administration or huge pharmacological doses.

Nevertheless, the interpretation of these observations has been revised by recent demonstration of changes in the distribution of changes in the distribution of exogenous IGF entering the vascular system, changes in the binding and receptor affinity [in tissues], higher levels, free IGF, in serum, and partial proteolysis of BPs, (among other changes] that together improve and maximize the bio-availability of the exogenous IGF, and increase or "facilitate" target tissues responses.

Thus, the concentration of serum total IGF is not necessarily an important indicator of IGF bio-availability.

Issue: The proportion of serum endogenous total IGF pool attributable to the ingestion of rBST milk-borne (exogenous) IGF is contentious.

JECFA contends that the milk-borne IGF contribution to serum IGF (< 0.1%) is negligible, and does not affect the of rBST milk.

The foregoing issues provide scientific and practical rationales for continuing the reviews of exogenous IGF in milk.

2. Data Sources for the Estimates

A. Estimates of exogenous IGF in blood and lymph are affected by

i) dosage (single vs. multiple),
ii) time-concentration curves;
iii) distribution, concentration and binding of serum BP
iv) period of observation; and
v) tests and essays used to detect exogenous IGF and endogenous IGF and BPs.

The above data reflect the mutual regulatory actions of IGF and their BPs, which can enhance the bio-availability of serum IGF. These data also affect the reliability of the estimates.

As expected, there is little compatibility among studies, with regard to test animal [or humans], mode and dose of IGF administration, or assays\tests used to detect exogenous IGF.

This explains the diversity [variance] in the findings; it also precludes a meta-analysis approach.

Instead, alternatives are presented. Of these, analysis of area-under-the curve for exogenous IGF did not vary appreciably.

B. Studies on the effects of exogenous IGF on endogenous IGF in human serum, lymph and tissues were largely IGF injection studies, either by intravenous, bolus, or subcutaneous (sc).

- The time-curves for SC are slower than the other modes, and the mechanisms for entering the circulation are much more complex.

Accordingly, only the IV Bolus data on humans were used here.

This may not reflect the concentration-time-curves for ingested absorption of IGF.

The oral [feeding] studies were mainly on animals, and species differences cannot be ruled out. This may partially explain the 10-fold difference in results [percentage exogenous of total bio-available IGF] between the estimates here and those made by JECFA.

Analytical Approach

The shift of IGF from smaller to large BP complexes, reported by several workers, was computed as follows:

- Increments in large complex IGF, over successive time points, represent the shifts from (a) free IGF [in serum exogenous or endogenous] during the first15 to 30 minutes, and then (b) from IGF of the small complexes.

Estimates of the pool of exogenous IGF crossing the capillaries to the interstitium/lymphatics is computed as a second step.

- Decriments in IGF in small complex over successive time points, minus the IGF shift to the IGF large complex, represent [a] crossing into lymph, and [b] degration.

- The [a] portion [into the lymph] is proportional to the IGF small complex concentration in the serum.

- The [b] portion can be differentiated over time. For short period of time, there is no degration.

4. Statistical fit

Statistics from the estimates, such as rates and percentages, show a reasonable fit with ratios and percentages reported in the literature; for example, crossing-to-lymph percentages of 20 to 40 percent have been reported, which is consistent with the 31 percent of this analysis.

Principles of activity and regulation of the IGF system

Use of a tracer IGF, analogues and recombinant IGF, has clarified IGF mechanisms.

Despite the incomparability among studies and the variation in research findings, patterns in IGF activities emerge that can form a scientific framework and for predicting the bio-availability of exogenous IGF.

Paramount is the regulation and disposition of IGF serum and tissues; these depend on dose, duration and mode of administration of the IGF.

Ultimately, exogenous IGF is associated with regulatory changes, which serve to increase IGF bio-availability.

The regulatory changes and principles listed below apply also to serum exogenous IGF, unless otherwise stated.

Principles

1. Availability of IGF BP binding complexes and their binding activity divide serum IGF into three distinct levels of bio-availability: very low [associated with the large ternary complex); moderate-to-high [associated with serum small complexes]; total and very high [associated with unbound, or "free" IGF].

2. Serum BP binding of IGF is active, not passive, and much more sensitive in humans then predicted.

3. In humans, free intact IGF can last much longer in serum than predicted.

   Exogenous IGF entering the vascular system binds with serum small complexes BP's first, and then shifts to large ternary complex.

4. The Spurs talks in a paragraph 5 period IGF is bio active only at the side of the target tissue, and only after it leaves the vascular system to bind the target cell receptors.

5. The above process represents the endocrine activity of IGF. IGF also has paracrine and autocrine activities which do not involve the vascular system, but which may still affect exogenous IGF through direct contact that may occur [e.g., intestinal tract] or indirectly through competition for the receptor binding on cell surfaces.

6. The serum large ternary complex is too large to cross the capillary barrier. Ninety-five percent stays in the vascular system, where it serves as a transport and storage system, and may help in targeting delivery of IGF.

   Small complexes of bound IGF and free IGF cross in and out of the blood, into the lymph, interstitium and target tissues. In the target tissues, they are a source of IGF delivered to the target tissue cells.

7. The exit of IGF from blood to tissues is very rapid.

8. The concentration of serum endogenous IGF [baseline] is constant and under homeostatic static equilibrium. Serum IGF is continuously replenished through the production of IGF in tissue entrances to the blood.

9. When external [exogenous] IGF enters a vascular system, there is a transitional stage of BP binding shifts and degradation, followed by a steady state and then a return to serum endogenous baseline. There are thresholds, saturation points and ceilings covering the rise and units and concentration of serum total IGF, and to a lesser extent, in the duration of the transitional stage.

10. Endogenous and exogenous IGF can modify and regulate its bio-availability, through auto-regulation and in synergy with the IGF regulatory system.

    This involves changes in activities of IGF and BPs, and in binding activity, redistribution of IGF among serum large and small complexes and in disassociation rates, induction of its [i.e., IGF's] own binding proteins [for serum binding], minor proteoloysis of BPs in large ternary complex, and up\downgrading of IGF cell-surface receptors.

11. Repeated doses of exogenous IGF can lead to "accommodation" of IGF regulatory activity and increased antigenic response in humans.

12. In the gastrointestinal tract, exogenous IGF remains intact much longer than predicted. Absorption of free, intact IGF is determined by concentration of IGF and receptor binding spaces available in the endovascular wall and intestinal mucosal [and not by the BP binding the IGF or present in the intestine].

Appendix A-3

Technical Notes

The production of estimates of bio-available IGF from ingestion of rBST milk raised three issues:

(A) The estimates are minimal values, insofar as:

- Absorption of milk is arguably much higher than 10%;
- The impact of extended or long-term consumption was not accounted for. Several researchers have reported changes in "area-under-the-curve," increased (and earlier) peaks in free IGF's, and changes in serum BP distributions, all related to one-week injections of IGF's in humans. Also, there is much longer survival of free IGF in serum, as well as in the gut, than that reported in some lab studies. Thus, despite the low percentages of exogenous IGF in the total IGF bioavailability, repeated daily doses over years are bound to multiply the change and their effects.

1. Estimates are affected by time-curves, the distribution and concentrations of B.P., and the tests used to measure IGF and B.P.

   There is little comparability among studies (test animal, or human, mode of IGF use), which precludes a meta-analysis approach. Instead, alternatives are presented. Analysis of area-under-the-curve did not change the estimates appreciably.

2. Studies on the effect of IGF in humans were largely injection studies, either intravenous Bolus, or subcutaneous.

   - The time-curves for SC are slower than the other modes, and the mechanisms for entering the circulation are much more complex.
   - Accordingly, only the I.V. Bolus data on humans were used here.
   - This may not reflect the concentration-time-curves of digestive absorption of IGF.

   The oral feeding studies were mainly on animals, and species differences cannot be ruled out. This may partly explain the 10-fold difference in results (% exog, of total bio-available IGF).

The shift of IGF from smaller to the large B.P. complexes, reported by several researchers, was computed as follows:

- Increments in large complex IGF, over successive time points, represent the shifts from (a) free IGF (in serum exogenous or endogenous) during the first 15-30 minutes, and then (b) from IGF of the small complexes.

IGF crossing the capillaries to the interstitium/lymphatics is computed as a second step.

- Decriments in IGF in small complexes, over successive time points, minus the IGF shift to the IGF large complex, represent (a) crossing into lymph, and (b) degradation.

  < The (a) portion (into the lymph) is proportional to the IGF small complexes concentration in the serum.
  < The (b) portion can be differentiated over time. For a short period of time, there is no degradation.

Lastly, statistics of the estimates, such as ratios and percentages, show a reasonable fit with ratios and percentages reported in the literature; for example, crossing-to-lymph percentages of 20% to 40% have been reported. This is consistent with the 30% analysis.

C Lieberman, S.A., Bukar, J. et al. Effects of Recombinant Human Insulin-Like Growth Factor - I (rhIGF-I) on Total and Free IGF-1 Concentrations, IGF-Binding Proteins and Glycemic Response in Humans. J. Clin Endocinol Metab., 1992; 75:30-36.

C Takano, K., Hizuka, N. et al. Repeated sc Administration of Recombinant Human Insulin-Like Growth Factor I (IGF-1) to Human Subjects for Seven Days. Growth Regulation 1991; 1:23-28.

Appendix A-4

Appendix Tables

Appendix Table A-1

Estimates of Endogenous (Native) Bio-available IGF in Human Serum and Lymph: Two Models Based on Distribution of Binding Proteins for IGF (IGF BP)

Total IGF	IGF in Serum Small BP Complexes			IGF in Large BP Complex			Serum Free IGF			A	B	C
ng	%	ng	Cross to Lymph	%	% Bio-avail	ng	%	ng	Cross to Lymph	Sum IGF in Small Complexes + Free IGF ng	IGF in Lymph ng	= A + B ng
MODEL I (GULER)												
1,225,000[a]	30	367,500	Even pro-portions IGF [b]	60	5	36,750	10	122,500	Even proportions IGF	490,000	245,000 [c]	735,000

Appendix Table A-1

Estimates of Endogenous (Native) Bio-available IGF in Human Serum and Lymph: Two Models Based on Distribution of Binding Proteins for IGF (IGF BP)

Total IGF	IGF in Serum Small BP Complexes			IGF in Large BP Complex			Serum Free IGF			A	B	C
ng	%	ng	Cross to Lymph	%	% Bio-avail	ng	%	ng	Cross to Lymph	Sum IGF in Small Complexes + Free IGF ng	IGF in Lymph ng	= A + B ng
				MODEL II (BINOUX; BAXTER)								
1,225,000	15	183,750	Even proportion IGF[b]	80	5	49,000	1[d]	12,250	Even proportions	196,000	245,000	441,000

Legend: a) Based on JECFA Report, (1999)

b) There is a partial barrier to BP in the small complexes (approximately 50KDa) but not to the IGF they bind. The proportions and concentrations of these IGF's are similar in blood and lymph.

c) IGF in lymph is reported as approximately 20% (average) of serum total IGF concentration. Lymph IGF pool: 1-225,000 ng x .20 = 245,000 ng IGF.

d) The percentage of serum free IGF has been measured as around 1% of total serum IGF; reports range from 1%-5%.

* Estimates for bio-available IGF from BP large complexes (150KD) were calculated for the data sheets, but were not included in the computations of the exogenous or endogenous values respectively; nor were the percentages included, unless otherwise stated.

Appendix Table A-2

Data Sheet for Table 1-1
Time Curve of BP Per Cent Distribution: Model 1

Exogenous 1GF from (Milk) i.e., 19,500 ng; 10% [a] absorption rate: IGF dose = 1,950 ng daily
Total IGF in serum: 1,225,000 ng

Time	IGF in Serum Small Complexes	Serum Free IGF	IGF in Serum Large Complex
Min. from start	**%**	**%**	**%**
From Data on i.v. Bolus Injection of IGF in Humans [b]			
0-5	60	7.6	32.3
5-20	53.5	1.2	45.3
30	37.9	0	62.1
60	35.1	0	64.9
90	26.9	0	73.1
120	16.8	0	83.2
180	12.1	0	87.9
240	0	0	100

Legend: a) Several authors have reported around 4% absorption rates, though there is more support for 10% absorption. Experiments using casein or other supplements orally have reported marked increases in absorption rate. The concentration of these supplements (to special milk preparations) are similar to that found in milk naturally.
b) Percentages are based on Guler Reports.

Appendix Table A-3

Data Sheet for Table 1-2
Time-Curve of BP Per Cent Distribution: Model II

Exogenous 1GF from (Milk) = 19,500 ng; 10% [a] absorption rate; IGF dose = 1,950 ng daily
Total IGF in serum: 1,225,000 ng

Time	IGF in Serum Small Complexes	Serum Free IGF	IGF in Serum Large Complex	Time-Curve Cumulative Distribution of Exogenous Total IGF in Serum
Min.	**%**	**%**	**%**	**%**
From Data on Oral Feeding of IGF (Animals)				
0-5	84	0	16	
15-20	84.2	0	15.8	1.9
30	84.7	0	15.3	7.9
60	84.4	0	15.6	21.2
90	84.5	0	15.5	36.7
120	84.1	0	15.9	55.9
180	82.3	0	17.7	77.5
240	82.7	0	17.3	98.4

Legend: a) Percentages are based on Donovan's reports and others.

NOTE: Time-curve of BP distributions are stable. The time-curve distribution of total exogenous IGF in serum is the inverse of that reported for i.v.:IGF administration.

Appendix A-5

IGF Bibliography

The bibliography is divided into six sections, each dealing with a specific topic.

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Appendix B:

Health Canada Expert Panel on Human Safety

1. Health Canada has wrongly implied that the Expert Panel on human safety was officially associated with the Royal College of Physicians and Surgeons of Canada. This was refuted by the Head of the Communications Section, Royal College of Physicians and Surgeons Pierrette-Leonard.[114]

2. Appendix 1 of information distributed to Human Safety Panel Members within their report[115] includes "Third Party Submissions" and uses the Toronto Food Policy Group Position Paper (August 1997) as an example. For the record, TFPC did not submit its position paper, or any further correspondence, to this committee because it would not review rbGH within a regulatory context. Therefore, the TFPC position paper was supplied by an alternative source.

3. The Expert Panel on Human Safety claims there is one exception to claiming human safety regarding rbGH in Canada (with no regulatory references), which is the anti-body response in the sub-acute 14 week rat study identified by the scientific rbGH GAPs analysis Team assigned Health Canada, and recommended that study be repeated. Therefore, until that request for the repeating of that experiment is completed, there can be no science-based claim by Health Canada that there are no human safety concerns.

[114] RbST Background notes, Royal College of Physicians and Surgeons of Canada, Nov. 18th, 1998

[115] Health Canada: Report on RbST, Part 1 and Part II, from Health Canada website http://www.hc.-sc.gc.ca/english/archives/rbst/humans/

Appendix C:

The Joint Expert Committee on Food Additives (JECFA)

The Joint Expert Committee on Food Additives (JECFA) has existed since 1955. It is the scientific advisory committee to the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) of the United Nations, and to Member Governments and the Codex Alimentarius Commission. JECFA's principal role is to assess human health risks associated with the consumption of food additives, and to recommend acceptable daily intake levels (ADI's) tolerable limits for environmental and industrial chemical contaminants in food, and maximum residue levels of agricultural chemical inputs in food, i.e., veterinary drug residues in meat and meat products. Membership in this committee is not permanent; rather members are appointed prior to each meeting.[116]

Two meetings of the Committee, the fortieth in 1993 and the fiftieth in 1998, evaluated rbGH as part of their review of submitted drugs.

Both times the JECFA repeated the same assessment error. JECFA does not comprehend nor pretend to understand that milk and dairy cattle could be under the protection of scientifically-established requirements for a particular nation's needs or specifications. One must read the fine print within a JECFA report to understand this point. JECFA decisions are based on collective views of an international group of experts, and do not necessarily represent the decisions or stated policy of the WHO or the FAO or the United Nations.[117]

Furthermore, the designations employed or presentations of material within a JECFA publication do not imply the expression of any opinion whatsoever on the part of the organizations participating in the International Programme on Chemical Safety concerning the legal status, authorities or boundaries of any country, territory, city or area.[118] JECFA does not have jurisdiction regarding any drug product's acceptability or use in any member country of the United Nations.

In matters relating to rbGH, the JECFA decisions are consistently flawed for three reasons:

1. JECFA conclusions are generalized, ignoring established scientific parameters within legislated

[116] Interim Report of the Standing Senate Committee on Agriculture and Forestry, rBST and the Drug Approval Process, Appendix II, page 28, March 1999

[117] WHO Technical Report Series 832, Evaluation of Certain Veterinary Drug Residues in Food, Fortieth report of the Joint FAO/WHO Expert Committee on Food Additives, 1993, front cover, fine print in the upper right corner.

[118] WHO Food Additives Series 41, Toxicological evaluation of certain veterinary drug residues in food, Fiftieth meeting of the Joint FAO/WHO Expert Committee on Food Additives, Preface, page vi

scientific mandates, on regulations and definitions used by the dairy industry. The latter are based on livestock husbandry principles and dairy product specifications, as presented in this paper, such as the definition of milk and the animals producing milk. These will vary between countries within the World Trade Organization (WTO) and the North American Free Trade Agreement (NAFTA). Assuming rbGH was safe for use, and did not affect the composition of milk, Canada could not allow the use of this drug because the Animal Pedigree Act is a defining statute for export of breeding stock within the North American Free Trade Agreement.[119]

2. The JECFA admits scientific variations in raw milk from dairy cows injected with the rbGH when compared to unmodified or normal cows, even after pasteurization. JECFA is not geared to rationalize a decision based on the "effect" (altered milk profile) "caused" by human intervention designed to reconfigure an existing animals' inherent properties (modification or adulteration).

3. Blindly incorporating a JECFA conclusion can in fact put countries in jeopardy of trade violations. In the case of rbGH, any country not checking the impact of the drug's review within assigned domestic regulatory responsibilities can be challenged for adulterated food, which is not a safety issue under Codex Alimentarius "Code of Ethics for International Trades."[120]

   This would be based on whether product specificity or integrity is established. Since Canadian regulations require raw milk to be the normal lacteal secretion from the mammary gland of the cow genus *bos*, then it behooves the regulatory agencies to ensure any dairy product exported from Canada is from normal raw milk, not abnormal lacteal secretion.

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[119] See Schedule 1 "Customs Tariff" section 1, Live Animals, Animal Products, Notes:
1. Any reference in this section to a particular genus or species of an animal, except where the context otherwise requires, includes a reference to the young of that genus or species.
Schedule 1. Chapter 1, Live Animals Supplementary Note:
1. For the purposes of headings Nos. 01.01 to 01.04 inclusive, the expression "purebred breeding animals" applies only to animals certified by the director of the Canadian National Livestock Records or the secretary or any other governing association incorporated under the Livestock Pedigree Act as being purebred, imported especially for breeding purposes.

Sections 01.01 to 01.04 are the tariff items under the FTA and the NAFTA and include Purebred Breeding Animals of the following species.
-live horses, asses, mules and hinnies
-live bovines
-live swine
-live sheep
-live goats
(See Article 401, of NAFTA, rules or origin.

[120] See Codex Code of Ethics for International Trade in Food, Article 4, General Principles; subject to the provisions of Article 5, no food should be in international trade which: 4.2(c) is adulterated; or (d) is labeled, or presented in a manner that is false, misleading or deceptive, [end clause]

Other failures of JECFA, specifically the Fiftieth Meeting (1998) include:

1. No Chronic or long-term safety data are shown.

2. Continual usage of the term "rbST treated;" cows injected with this drug are not sick, and it has no therapeutic uses. The use of hormones in beef cattle as growth promotants or production enhancing drugs is called "implantation," and the cattle are "implanted," **not treated.**

3. JECFA concludes that the use of rbGH, in accordance with good veterinary practice, will not pose a dietary hazard to human health.[121] Good veterinary practice does not include the use of a drug that has over 20 side effects, all detrimental to animal health noted on the warning label of an rbGH variant known as "Posilac" produced by the Monsanto Corporation. This is serious cause for a regulatory review.[122] [123]

4. Failure to provide regulatory background data on antibiotic residues, in accordance with United States Food and Drug Administration standards. The JECFA claim of insignificant levels of milk discarded due to antibiotic use is not valid until proof is shown that the drug tolerance levels for antibiotics in milk set by the FDA in 1997 are the same as they were in 1993. If these tolerances are the same or lower, then JECFA has no scientific grounding for its conclusion.

5. Failure to be consistent and relevant regarding the hormone levels of rbGH and IGF-1, as well as including the use of the very same papers proven to be inaccurate earlier in this paper, (Juskevich and Guyer, Groenewegen, etc.) and dismissing the pasteurization issue.

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[121] JECFA, p143,n2. The non-therapeutic use of rbGH in an uncontrollable environment (dairy farm economics, and dairy cow genetics dictated by the dairy farmer), allowed by a veterinary should be classed as Iatrogenic disease. Defined as illness resulting from professional activity of physicians or other health professionals (Dr. John Last, Dictionary of Epidemiology). The international classification of diseases (WHO) also includes adverse effects of drugs prescribed by a professional. Since rbGH can be prescribed by veterinarians, and the drug and its mediator, (both imputed to have harmful as well as beneficial effects) thereby allowing entry into the food chain, then illnesses yet to be determined would be designated Iatrogenic diseases through a chain reaction.

[122] This point was raised by Veterinary Dr. Herman Abmayr, in reviewing the history of medico-legal definitions (European Union, 1994). Two points made by Dr. Abmayr were that the word medications was too vague (proposed changing to veterinary medication and production enhancing hormones). His second point was the failure to correct the definitions would result in a conflict under Article 11, paragraph 1 of the European Union because the non-therapeutic use of the drug could not be placed on the same plane as medication, which rbGH is not.

[123] See Veterinary Act, Ontario Reg. 1015-1103. Vol. 8, 1990, non-therapeutic use is not associated with the term "treated" or the list of allowable mobile veterinary practices in section 14, sub-section 7

6. No controlled assessment of the dilution factor of IGF-1 in milk being exposed to specific population models. This is a failure to establish relevant comparisons of IGF-1 levels in milk from rbGH modified cows versus normal cows. The use of grocery store samples is not grounds for a scientific basis of safety. The use of Eppard, et al 1994[124] is flawed because it is not a sound diagnostic tool for certain exposure groups, specifically farm families drinking rbGH milk right from their bulk milk tank and vulnerable members of the population such as cancer patients. Eppard's study compared IGF-1 levels in milk obtained from a grocery store between two groups of milk: (i) labeled as not from cows injected with rbGH and (ii) milk from unlabeled milk; the assumption, not fact, would be that rbGH modified cows milk would be in the unlabeled milk cartons.

   The study conclusion of a slight increase of IGF-1 levels (4.4 ng/ml vs. 4.7 ng/ml) expressed no increase of IGF-1 after the launch of rbGH. This statement has to be flatly rejected until the following evidence is shown.

   A) How many herds were using rbGH that supplied that particular dairy processor(s) that were in the retail store?

   B) How many cows were injected by the farmers using the drug in that region supplying said processor(s) that Eppard used in his study?

   The JECFA itself asked the same questions, yet included this reference as a valid point regarding IGF-1 levels. Therefore, TFPC must question the controls applied by JECFA to prove a point, especially when JECFA has shown no understanding of individual country's requirements.

   The World Food Summit in 1996 created an action plan[125] which states in part: " to this end governments in partnership with all actors of civil society, as appropriate will apply measures, in conformity with the agreement on the application of Sanitary and Phytosanitary Measures and other relevant international agreements that ensure the quality and safety of food supply, particularly by strengthening normal and control activities in the area of human, animal and plant health safety." Accepting the JECFA judgement does not conform to the requirements of this action plan.

JECFA decisions in the matter of rbGH do not necessarily conform to normal or control activities for individual member countries, specifically Canada's dairy industry. Proponents of rbGH are too quick to utilize

[124] P.J. Eppard, R.J. Collier, R.L. Hintz, J.J. Veenhuizen, C.A. Baille, Survey of milk insulin-like growth factor in retail milk samples. Unpublished report No. 100-USA-COW-RJC-94-074, from Protiva, Monsanto Company

[125] World Food Summit, Rome Declaration of World Food Security and World Food Summit, Plan of Action, page 15, section 21, objective 2.3, 1996

the JECFA as the end of a credible decision-making process. Sensibly, JECFA is just a beginning.

Appendix D:

Bakewell Revisited
Bakewells' Ten Rules (Short Version, compared to Bakewells' Principles)[126]

1. Correct training of the eye and judgment in the anatomy and physiology of the animal.

2. The correlation of the several parts, one to the other.

3. The selection and mating of animals with a view to the fullest development of the most valuable parts, according to the use intended.

4. Selection with a view to the perpetuation of essential qualities to induce form, symmetry, high feeding qualities and great vigor of constitution.

5. Feeding with reference to early maturity for giving development in the least possible time.

6. Shelter and warmth indispensable to perfect development.

7. Variety of food is essential and this according to the age of animal.

8. A strain of blood once established, never go outside of it for a new infusion.

9. The most perfect care and regularity in all matters pertaining to feeding and stable management

10. Kindness and careful training absolutely necessary with a view to the inheritance of high courage, combined with docility and tractability.

Note: The reader will notice a huge variation between this page and the following pages. It is noteworthy that this concise version though clear, lacks the nuances in the earlier version of his principles.

[126] This version was printed in the Livestock and Complete Stock Doctor Encyclopedia, A.H. Baker, Dean and Professor of Theory and Practice, Chicago Veterinary School, Hon. J. Periam, author Cyclopedia of Agriculture,. Hon. W.D. Hoard, publisher Hoard's Dairyman, co-authored with representation from the University of Guelph G.E. Day, Professor of Agriculture and Farm Superintendent, H.H. Dean, Professor of Dairy Husbandry, J.H. Reed, Professor of Veterinary Science, W. R. Graham, Manger and Lecturer Poultry Department, pg. 644, 1914

The Principles of Bakewell (Long Version)[127]

1. *Beauty of Symmetry or Shape*- in which the form is *so* compact, that every part of the animal bears a pleasing proportion to the rest. This, however, is so intimately connected with the second principle that we comprise them both in the same description.

2. Utility of form- Both beauty and utility demand that the head of the cow and the ox should be fine and small, gradually tapering towards the muzzle. This is a great point of beauty, and it is also connected with utility, for there are few good milkers, or good feeders, who have not this fineness of muzzle. A thick clumsy head denotes a want of refinement and quality. The neck, towards the setting on the head, should be finely shaped, although it may be allowed somewhat rapidly to thicken towards the shoulder and the breast. The chest is an all important part. It should be deep and broad, and should be carried forward to the fullest extent. The back should be broad as well as level, and the barrel ribbed almost to the hip. There should not only be room for the heart and lungs before, but for the capacious haunch behind. The loins should be wide at the hips, but not to prominent, for there is the most valuable meat. The thighs should be full and long and near together, and the legs should be short almost to a blemish. The bones of the legs should be small, but not disproportionately so, and the hide mellow and fairly loose-everywhere covered with hair, soft and fine, but not effeminately so-feeling like a soft rug doubled in the hand. Such is the animal in which the qualities of beauty and utility blended.

3. The flesh, or texture of the muscular parts, is a quality that necessarily varies according to the age and size of cattle, yet it may be greatly regulated by attention to the food employed for fattening them. It si best shown in the flesh being marbled, or have the fat and lean finely veined or intermixed, when the animals are killed; and while alive, a firm and mellow feeling.

4. In *rearing of live stock* of any description, it should be an invariable rule to breed from fine boned, straight backed, healthy, clean kindly skinned, and barrel shaped animals, having clean necks and throats, and little or no dewlap; carefully rejecting all those which have coarse legs and roach backs, or with much appearance of offal. As some breeds have a tendency to develop great quantities of fat on certain parts of the frame, while in others it is more mixed with the flesh of every portion of the animal, this circumstance will claim the attention of the breeder as he advances in the knowledge of his business.

[127] The Complete Grazier and Farmer's and Cattle Breeders Assistant, A compendium of Husbandry, originally written by W. Youatt, Member of the Council of the Royal Agricultural Society of England, Thirteenth Edition, by W. Fream, University of Edinburgh , page 86-88, 1893

5. In *purchasing of cattle*, whether in a lean or fat state, the farmer should on no account procure them out of richer or better grounds than those in which he intends to turn them. He should select them either from stock feeding in the neighborhood, or from such breeds as are best adapted to the nature and situation of the soil. As an example, it may be noticed that Highland cattle with often thrive on English pastures that are unsuited to the most delicate animals.

6. *Docility of Disposition*- is an object of great moment; for, independently of the damage committed by cattle of wild tempers on fences, fields,&c., it is an indisputable fact that *tame beasts require less food to rear support and fatten them*. Every attention should therefore be early paid to accustom them to docile and familiar; and gentle, kindly, equable treatment will most effectually conduce to this end.

7. Hardiness of constitution, particularly in bleak and exposed districts, is a most important requisite.. It usually depends on form; all animals with fine arched ribs, and wide chests and backs are more likely to prove hardy than those having their fore quarters narrow. There is a rather prevalent opinion that white mark is a delicacy of constitution; but the wild cattle of Chillingham are invariably that colour, and the highest bred Herefords are distinguished by white faces.

8. Connected with the hardiness of constitution is early maturity, which, however, can only be attained by feeding cattle in such a manner as to keep them constantly in a growing state. Beasts and sheep with this prosperity, and thus managed, thrive more in one year than they would do in two if they had not sufficient food in the winter.

9. There is in some animals a *kindly disposition* to accumulate fat on the most valuable parts of the carcass at an early age, and with little food, compared with the quality and quantity consumed by others. On this account smaller cattle have been recommended as generally having a stronger disposition to fatten, and as requiring, proportionately to the larger animal, less food to make them fat; consequently, a greater quantity of meat can be produced per acre. "In stall feeding,"- the nature, method, and advantages of which will be stated, in a subsequent chapter,-- it has been remarked that "whatever may be the food, the smaller animal pays for most of that food. In dry lands, the smaller animal is always sufficiently heavy for treading, in wet lands he is less injurious"[128] This opinion, however, is combated by some very able judges, who still contend that the largest animals are the most profitable. They doubtless may be so on strong land; but the smaller animals will thrive on soils where heavy beasts would decline.

[128] Journal of the Bath and West of England Society, Vol. X, p. 262

Discussion of Bakewell:

Many of the words and principles of Bakewell listings are still incorporated today in judging, cattle manuals, codes of ethics for animal handling and lists of desirable animals to work with. The caution that TFPC wishes to present to the ideal cattle type stated in the preceding pages is they are environment-specific (England and Scotland). Also, it should be known that Bakewell's actual work in breeding, though fundamentally sound given the time period, fell into disfavour as breeders advanced their knowledge.

Scientific stock-breeding began after the cessation of warfare between England and Scotland at the battle of Culloden in 1746.[129] With permanent peace at hand, stock breeders and Bakewell began the long-term advancement of livestock breeding.

However, Bakewell's success was based on the term " breed the best from the best" or "like begets like," which in reflection by later generations meant *inbreeding*. As pointed out by many stockmen such as Marshal 1932,[130] this method is only to be carried on by experts, and is most dangerous for amateurs.

The irony of hormones is that they are an emotion-based response to civil unrest, i.e., revolution or war, to cure actual or potential food shortages. Such was the background of the early Soviet trials of the late 1920's. Proponents of rbGH argue that modern hormone use is nothing new. Our response is the question: why were the Soviets intent on modifying cattle to improve production? Russian history shows the severe strife caused by the First World War, the Russian Revolution, the creation of state farms with inexperienced workers, which led to starvation. The second push in hormones was by the United States Department of Agriculture in 1942, during the Second World War. It was then hoped that the new synthetic hormones would be available to alleviate certain food shortages due to wartime carnage of livestock.

Bakewell's success with breed improvement was born out of peace, which allowed farmers time to observe, appreciate and allow development of the their livestock, thereby creating a scientific progression based on sound measurement. Ergo, the conflict of wartime science (reactive) versus peacetime science (pro-active).

The results of peacetime scientific disciplines are evident. But they are in danger of being lost in a fog of technological mismanagement.

[129]The Complete Grazier and Farmer's and Cattle Breeders Assistant, A compendium of Husbandry, originally written by W. Youatt, Member of the Council of the Royal Agricultural Society of England, Thirteenth Edition, by W. Fream, University of Edinburgh , page 16-17, 1893

[130] Shorthorn Cattle in Canada, Duncan Marshall, 1932

Appendix E:

Recommendation 3

3. That the indiscriminate use of any hormone on dairy cattle be prohibited.

Explanation:

TFPC uses the term "indiscriminate' to indicate "use without need." The milk and meat withdrawal times for hormones in Table 3 have specific therapeutic uses[131]. It is proven that the therapeutic use of hormones is not conducive to stated objectives. They have helped prevent inferior livestock from being culled. Farmers are not trained to differentiate and record animals they know are problem breeders requiring the drug.

Therefore our recommendations is that the record system already in place, through milk recording agencies, help farmers transmit that data into the actual sire proofs to be viewed by farmers. Veterinarians can assist in this matter as well.

The point is that this information must be used and promoted through the breed associations, so that sires with a high degree of reproductively unsound daughters are exposed and those sires removed.
A breeding code for daughter conception should be a prime component of a sire proof, yet for over 40 years this basic requirement of breeding value has not been applied in the Canadian Artificial Insemination Industry.

If properly and patiently incorporated over time, the need for hormones may be reduced greatly because the cattle once again will be evaluated for true genetic performance. This is why TFPC will not propose an outright ban on hormones, because it could cause shell shock to many dairy farms. However, it would not hurt to set a time frame of three generations of proven sires. Each generation requires seven years to be proven, and allowing a three lactation life-span of daughters means a target date of 2030. Per capita use of hormones in the cow population can be evaluated by percentage then in comparison to now.

Finally, to establish that modification of a cow creates a different milk yield than the environment, which proponents of rbGH have failed to grasp, we produce tables 9 and 10 to illustrate the point that rbGH is not like any other current technology for obtaining milk yields (such as feed supplements or total mixed rations).

Our case to prove inherent modification is demonstrated in the following scenarios:

[131] With the exception of artificially stimulating the ovaries of a cow to super ovulate and produce large quantities of eggs for fertilization. This is known as embryo transplant, where the donor cow produces many eggs hopefully fertilized, withdrawn from the donor cow and each egg implanted into what is known a recipient to carry the embryo full term. This is minimally used in the national herd and is actually considered an advancement to increase the number of superior cattle.

Table 9

Scenario No. 1

If we had the ability to move a cow to the three basic management programs available in Canada: The energy needed to produce these management scenarios increases, from 1 being lowest to 3 being highest.

Management No. 1	Management No. 2	Management No. 3
- Seasonal pasture - Mixed grain ration - Mixed first cut hay	- Zero Grazing - Prepared feed - Ensiled Forages	- Total Confinement - Total Mixed Ration
She produces 7,000 litres of milk	She produces 8,500 litres of milk	She produces 9,800 litres of milk

Question: Did the cow change?

Answer: No. The environment was modified, not the cow. The argument of production variability as an expression of genetic influence is null and void. The cow clearly showed she was genetically capable of withstanding the production system and able to produce according to **environment**.

Table 10

Scenario No. 2

Taking the same three management approaches mentioned above and three different cows of equal body conformity, butterfat and protein content.

Management No. 1	Management No. 2	Management No. 3
- Seasonal pasture - Mixed grain ration - Mixed first cut hay	- Zero Grazing - Prepared feed - Ensiled Forages	- Total Confinement - Total Mixed Ration
Cow A Makes 9,000 litres of milk	Cow B Makes 9,000 litres of milk	Cow C Makes 9,000 litres of milk

Question: Which is the superior cow?

Answer: Cow A. Though the level of production is constant in variable environments, Cow A proves superior NET (Net Energy Transfer) due to the lowest input of energy (relating to time for cropping, fuel, maintenance) to produce a litre of milk; therefore a more desirable cow to breed from for profit.

To inject rBGH into any of the above cows produces inherent modification. The human intervention of injecting a production hormone will make her milk more than was genetically (via breeding) possible under any environmental level of management.

Appendix F:

Table 11

Flavours and Odours Transmitted in Milk from Ingested Feeds

Feed	Amt. /lbs.	Interval pre-milking	Flavour and odour resulting in milk	Ref.#
Corn Silage Milking in strong silage atmosphere	-----	-----	Silage flavour in only 1/4 of samples, less effect than commonly supposed	1
Corn silage	15-15	l hour	Definite silage odour in all cases	1
Corn silage	15-25	ll hours*	Very slight silage flavour in 60% of samples, flavour is rather pleasant and not considered detrimental	1
Corn silage, spoiled (top)	5	1 hour	Strong flavour resembling garlic	1
Alfalfa silage	5	1 hour	Definite flavour in all cases	1
Alfalfa silage	15	1 hour	Very definite flavour, Rejection by consumers possible	1
Sweet clover silage	5	1 hour	Definite flavour in all cases	1
Sweet clover silage	15	1 hour	Very objectionable flavour in all cases	1
Soy bean silage	5	1 hour	Definite flavour and odour	1
Soy bean silage	15	1 hour	Very definite flavour	1
Turnips	15	1 hour	Objectionable flavour	2
Turnips	30	1 hour	Very objectionable flavour	2
Turnips	30	11 hours*	No flavour or odour	2
Green alfalfa	15	1 hour	Pronounced flavour	3
Green alfalfa	30	1 hour	Very pronounced flavour	3
Green alfalfa	30	3 hours	Slight flavour	3
Green alfalfa	30	5 hours	Practically no flavour	3
Green alfalfa	30	11 hours	No flavour effect	3
Green corn	25	1 hour	Only a slight flavour. Not objectionable	3
Green corn	25	11hours*	No flavour effect	3

*Estimated as 11 hours where feeding was immediately after the previous milking.

Table 11

Flavours and Odours Transmitted in Milk from Ingested Feeds

Feed	Amt. /lbs.	Interval pre-milking	Flavour and odour resulting in milk	Ref.#
Green rye	15	1 hour	Only slight flavour. Not objectionable	4
Green rye	30	1 hour	Slightly more flavour. Not objectionable	4
Green rye	30	11 hours*	No flavour effect	4
Green cowpeas	15	1 hour	Some effect on flavour. More with green rye	4
Green cowpeas	30	1 hour	Definite flavour	4
Green cowpeas	30	11 hours*	Practically no flavour effect	4
Cabbage	14.3	1 hour	Objectionable flavour	5
Cabbage	24	1 hour	Very objectionable flavour	5
Cabbage	25	11 hours*	Very slight flavour. Detection doubtful	5
Potatoes	14.8	1 hour	Slightly abnormal flavour	5
Potatoes	29.3	1 hour	More pronounced flavour, but still slight	5
Potatoes	28.7	11 hours*	No flavour effect	5
Beet pulp	30	1 hour	Only slight flavour	6
Green oats	30	1 hour	Only slight flavour	6
Pumpkin	30	1 hour	Practically no flavour effect	6
Carrots	30	1 hour	Practically no flavour effect	6
Sugar Beets	30	1 hour	No flavour effect	6
Rape	30	1 hour	Decidedly objectionable flavour	6
Soy beans	30	1 hour	Improved flavour	6
Kale	30	1 hour	Decidedly objectionable flavour	6
Alfalfa hay	36,561	30 min.	Flavour noticeable	7
Alfalfa hay	36,561	2 hours	Flavour in milk at its height	7
Alfalfa hay	36,561	4 hours	Flavour only noticeable in some cases	7
Alfalfa hay	36,561	5 hours	No flavour effect	7
Tankage	2 ½-4	1 hour	No flavour effect	8

Table 11				
Flavours and Odours Transmitted in Milk from Ingested Feeds				
Feed	**Amt. /lbs.**	**Interval pre-milking**	**Flavour and odour resulting in milk**	**Ref.#**
* Estimated as 11 hours where feeding was immediately after previous milking				

Table 11				
Flavours and Odours Transmitted in Milk from Ingested Feeds				
Feed	**Amt. /lbs.**	**Interval pre-milking**	**Flavour and odour resulting in milk**	**Ref.#**
Green alfalfa juice**	5-6 qts.	15 minutes	No flavour	9
Green alfalfa juice**	5-6 qts.	20 minutes	Definite flavour	9
Green alfalfa juice**	5-6 qts.	45-60 minutes	Flavour in milk at its height	9
Green alfalfa juice**	5-6 qts.	2 hours	Slight flavour	9
Garlic	½	1 minute	Garlic flavour detected by some judges	10
Garlic	½	4 hours	Very objectionable garlic flavour	10
Garlic	½	7 hours	Practically no flavour	10
Garlic odour inhaled by cows for 10 minutes	-----	2 minutes	Strong flavour in milk	10
Garlic odour inhaled by cows for 10 minutes	-----	90 minutes	Practically no flavour	10
** Expressed from 25 pounds of green alfalfa after freezing to rupture the cells				

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Appendix G:

Milk Production: How far have Canadian Dairy Farmers Come?

This section is designed to take a snapshot of historical points and show productivity gains in the Canadian dairy herd. For practical purposes, the dairy breed known as the Holstein, which represents 95 percent of the registered national dairy herds, shall be used[132] in tables 15-19. The following tables are from cattle and production records that are registered under the Animal Pedigree Act, and the Record of Performance Program accrediting milk records by the federal government and/or Provincial Dairy Herd Improvement Associations.

The following tables (11-19) show the level of milk production has not increased vertically over the past decades, from animals chosen to influence genetics in a dramatic manner influencing the national herd. Rather, improvement is based on lateral increase in the number of cows capable of achieving a provable plateau of milk production.

The cattle and milk records listed in tables 15-18 are from one artificial insemination unit(farm co-ops that house bulls for the purpose of collecting semen to be distributed to their members) as a focal point to compare the considered-best genetics helping influence breed improvement. A.I. studs incorporate a mandate to use the best cows for type (body conformation according to a standard) and production as the mothers of bulls entering the stud.

In 1993, Canada was fourth in the world for production per cow. A comparison table shows the top four countries, with production levels assessed by testing programs only, 305 day lactations, all breeds included.[133]

Table 11

Country	Kilograms milk (305 Day Records)	% of national herd on test
#1 Israel	10,136	52.1
#2 United States	8,382	30.2
#3 Japan	8,130	33.4
#4 Canada	7,988	61.2

[132] Dairy Improvement Statistics, 1994, Agriculture and Agri-Food Canada

[133] Ibid, page 42

Canada is not lacking in milk production capability. This table has empirical quality no longer available, due to rbGH use in the United States since 1994. It should also be noted that the higher herd averages (Israel and Canada) on test (milk recording) gives greater reliability to these countries' figures.

Using an Ontario A.I. Stud as a base due to its prominence in the history of dairying, and, using the average production of dairy cows on a testing program, and, using the first group of 1915 national milk recorded daughters of registered sires as a base, we see the following:

Table 12

Group (305 Day Records)	Kilograms of Milk	+ or - from the base
1915- 624 dairy cows on Record of Performance Average	5,799	0
1946 - 24 sires with 50 daughters each (ROP)	6,475	+676
1984 - the average was	6,842	+683
1993 - the average was	8,193	+2,394

If we compare the increase of bull mothers' production averages in table 14 to the increase of A.I., sires, we see a parallel proximity of achievement +2314 Kg. of milk (table 19) +2394 Kg. of milk (table 12)

The following table displays actual national milk production levels from 1956 to 1993.

Table 13	
Year	**Avg. Kg. Milk Produced Per Cow (305 Day Records)**
1956	4,843
1957-58	4,813
1958-59	5,050
1959-60	5,182
1960-61	5,083
1961-62	5,148
1962-63	5,235
1963-64	5,221
1964-65	5,333
1965-66	5,359
1966-67	5,511
1967-68	5,581
1968-69	5,632
1969	5,730
1970	5,923
1971	5,745
1972	5,947
1973	5,860
1974	5,784
1975	5,856
1976	6,037
1977	6,127
1978	6,241
1979	6,457

Table 13 (Con't)	
Year	**Avg. Kg. Milk Produced per Cow (305 Day Records)**
1980	6,479
1981	6,513
1982	6,562
1983	6,702
1984	6,842
1985	6,973
1986	7,086
1987	7,128
1988	7,348
1989	7,538
1990	7,625
1991	7,717
1992	8,028
1993	8,193

Information Source: Stats Canada, the Canadian Milk Recording Board and the Dairy Animal Improvement Statistics Report 1994, (Agriculture and Agri-Food Canada). The production levels listed are based initially on the Record of Performance Program and are 305 day lactation periods.

They do not include unofficial milk record averages.

Table 14

A Snapshot Comparison of Production Averages Using Table 15 as a base

Table Number	Year	Average Kilograms of milk produced	Average Kilograms of fat produced	+/- Kilograms milk	+/- Kilograms of fat
15	1949-50	9,529	375	0	0
16	1968	9,418	358	-111	-13
17	1975	9,827	390	298	15
18	1986	9,833	408	304	33
19	1993*	11,843	491	+2,314	116

* Denotes an increase in management techniques over previous decades. It is obvious that a steady and gradual rate of increase milk production has occurred in the national herd. This can be accredited to the artificial insemination industry which has helped disperse genetics at one time unavailable to the average farmer due to economic or distance restraints.

The Canadian Artificial Insemination Industry was started in 1942 by the Waterloo District Jersey Club in the province of Ontario. The Oxford County Holstein Breeders Association started in 1946, and the earliest catalogue secured for this stud was 1949-1950. This year will be used as a statistical base to assess any movement in production levels. (As there were and still are several artificial insemination co-operatives and companies that co-existed at the same time, it is our intent only to show how important registration numbers and milk records are to empirical genetic decisions to prove breeding value.)

Table 15

Oxford County Holstein Breeders
Artificial Insemination Unit,
Woodstock, Ontario, 1949-1950 Sire Catalogue

1st 10 Canadian Dams Listed- Best Milk Record

Name of Cow	Registration number	Age of lactation (Years)	X= times per day milked	Kilograms of milk 305 days	Kilograms of fat 305 days
Hartholm Lady Korndyke	215751	7	2	8,180	312
Raymondale Margie	616083	2	3	8,587	295
Locust Lodge Inka Queen	390127	8	NA	9,831	390
Elm Snowflake	387804	5	3	8,578	335
Elm Sylvia Colantha	323061	3	NA	12,762	469
Montvic Bonheur Emily	377754	5	NA	8,102	324
Locust Lodge B Colantha	519821	4	NA	9,244	377
Elm Flora Colantha R	449733	5	NA	9,211	415
Princess A Texal Fayne	403894	5	NA	11,629	469
Duchess of Elmcroft	543068	3	NA	9,135	365
Average Production 9,529 Kg. milk 375 Kg. fat					

Table 16

Oxford and District Cattle Breeders Association, Woodstock, Ontario, 1968

1st 10 Canadian Dams Listed- Best Record

Name of Cow	Registration Number	Age of lactation (years)	Times per day milked	Kilograms of Milk 305 days	Kilograms of Fat 305days
Browns Mistress Annette	513326	7	3	9,217	364
Baker Montvic Cav. Nig	757486	5	3	9,807	334
Vinedale Dekol Sue	929296	9	NA	8,871	362
Glenalcomb Supreme Dora	781990	10	2	9,378	324
Maple Heather B Finest	853595	8	2	8,395	336
Denfield Dewdrop Supreme	768454	5	2	12,424*	496
Greenwood Reflection Patsy	1592396	3	NA	7,568	310
Elkur Ideal Finderne	960518	7	NA	10,370	374
Windylea Nancy Lou	904759	8	NA	9,763	339
Marldale Princess Joy	1239801	4	2	8,388	343

Average Production 9,418 Kg. milk 358 Kg. fat * indicates a 365 day record

Table 17

Oxford and District Cattle Breeders Association Changed with amalgamation to Western Ontario Breeders Inc. (WOBI) (1975)

1st 10 Canadian Dams Listed- Best Record

Name of Cow	Registration Number	Age of Lactation (years)	Times per day Milked	Kilograms of milk 305 days	Kilograms of Fat 305 days
Downalane E Empress	1325135	7	NA	8,902	360
Malvoma Pabst Royal Duke	1214195	8	NA	9,417	344
Almamallek Haven Nelle	1468146	8	3	13,989*	521
Agro Acres P Pansy	1782508	6	NA	9,123	382
North Leeds Citation Girl	1641739	6	3	19,512	423
Bonnie Roburke Franco	1315986	8	NA	8,366	317
Viabest Dillis Citation	1603796	6	NA	9,473	364
Reflection Rose Queen	1560148	11	NA	8,403	377
Hi-Port Norma Triune	1525908	9	NA	10,337	436
Jewel Texal Dianne	1271335	6	NA	9,748	381

Average Production 9,827 Kg. Milk 390 Kg. fat *indicates a 365 day record

Table 18

Western Ontario Breeders (1986)

1st 10 Canadian Dams Listed- Best Record

Name of Cow	Registration Number	Age of Lactation (years)	Times per day milked	Kilograms of milk 305 days	Kilograms of fat 305 days
Medway Bonnie Mryna	2226003	8	NA	8,508	322
Cherrylane Marquis Sarah Lee	2636203	5	NA	11,222	474
Sunnylodge Dolly R. Ana	2480537	11	NA	9,556	389
A Sleepy Hollow Marq I	2937273	4	NA	9,290	437
Almerson Marquis Echo	2194243	6	NA	7,990	336
Donnandale Prestige Lulu	3216467	5	NA	8,352	336
Doriscroft Telstar Agat	2320559	9	NA	12,292	493
Wykholme Dewdrop Arlene	3112693	7	NA	9,246	400
Meadowbridge C. Harriet	2575563	5	NA	9,246	400
Haanview Peggie Nettie	1976476	11	NA	11,869	508
Average Production				9,833 Kg. milk	408 Kg. fat

Table 19

This table is based on the All Canadian Holstein Sires Catalogue from 1993, which was the result of the individual A.I. units sharing semen.

1st 10 Canadian Dams Listed - Best Record

Name of Cow	Registration number	Age of lactation (years)	Times per day Milked	Kilograms of Milk 305 days	Kilograms of Fat 305 days
Duregal Rivalty Valiant	3637287	3	2X	8,955	376
Spring Farm Astro Anna	3169221	8	NA	17,963	761
Hanover Hill T Barb- Alt	2878107	8	3X	12,635	513
A Mil-R-Mor Roxette	3567417	7	2X	9,949	464
Hanover Hill Shiek Barb	NA	7	2X	12,653	527
Peartome Thunder Joy	3335869	6	2X	11,388	489
Maplewood Shiek Betsy	3427918	4	NA	11,145	494
Startmore Chanel	3602443	5	NA	12,141	452
Sunnylodge Elev Jan	NA	6	2X	10,608	433
Madawaska Shady	3511527	3	NA	11,000	410
Average Production 11,843 Kg.milk 491 Kg. fat					

This significant increase in production shown in this table must be tempered by knowing increased feed management practices that were unavailable in prior decades to the degree we see in today's dairy farms.

The previous tables exemplify three things:

1. Registration numbers on lactating cows chosen to provide superior sires from the dairy breed databases

2. Milk records of cows with proven sons that advanced cattle quality on the nations' dairy farms

3. That there is a long term plateau of milk production that can propel a breed forward not vertically but rather horizontally. More cows that can produce higher levels of milk as demonstrated by the gradual and steady increase in the national averages over the 37 years within Table 13.

The work of Robert Bakewell is reflected well here as breed improvement in milk production is proven. It is also clear that the pioneers in dairy breeding exerted a strong influence by allowing time to appreciate and observe animal improvement.

In today's hurry-up society, it is refreshing to see long term success paced properly, as the Canadian dairy industry is capable of doing. However it is time to question whether the Canadian dairy industry will return to maintain and uphold the very disciplines that have created such as stable direction of progress. Or will this industry expire due to indifference of attention to fundamental details?

Appendix H:

Explanation of Genus *Bos*/*Taurus*

Cattle belong to the species Mammalia, the order of Arteriodactyla (even-toed animals)[134] and belong to the family Bovidae (meaning ox kind). Baker et al 1914[135], and Manning[136] 1881 make the distinction that genus *Bos* refers to the wild state, such as the African Buffalo, the North American Bison, whereas, genus *Taurus* refers to domesticated cattle[137]. The combination of genus *Bos/Taurus* in respect of the two parameters is furthered by Purdy, 1987, who states that *Bos Taurus* includes the ancestors of European cattle[138]. The cattle of Europe, from which Canadian dairy cattle originate, emanate from two distinctive classes of *Bos*, characterized by the shape of the skull:[139]

1) *Bos longifrons*, or as some authors prefer *Bos sondaicus*, (broad head, short horns) which is well represented by a breed of dairy cow known as the Jersey;

2) *Bos primigenius*, (long narrow head, middle horn length) which is represented as an example, by the dairy breed known as Holstein.

The origin of domesticated cattle are from the wild cattle that survived by the breeding of the fittest male(s) to the fittest female(s) in the environment they were naturally exposed to by area or migration patterns. Domesticated cattle were bred for work and propagation of future domesticated cattle, becoming known, as with other domesticated species, as livestock.

The above considerations are the grounding for our request to have *Bos* and *Taurus* combined in our proposal to amend the definition of milk.

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[137] See Footnote 125 and 126

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3. High Heat-Short Time

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